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CONTENTS

Diabetic retinopathy ..... *Jonas S. Friedenwald* 1187
Treatment of leukomas preceding keratoplasty ..... *Louis Paufique* 1200
Epibulbar tumors ..... *J. E. Ash* 1203
Ewing's tumor of the orbit ..... *Fred Harbert and George L. Tabor, Jr.* 1219
Streptothrix and conjunctivitis ..... *Frederick H. Theodore* 1225
ACTH in glaucoma ..... *E. M. Blake, R. M. Fasanella, and A. S. Wong* 1231
Contact lenses in keratoplasty ..... *Adrien Fritz* 1236
Nondiabetic lipemia retinalis ..... *Joseph J. Groom and C. W. Rucker* 1238
Effects of microwave diathermy ..... *Louis Daily, Jr., ...K. G. Wakim, J. F. Herrick, Edith M. Parkhill, and W. L. Benedict* 1241
Toxoplasmosis ..... *Albert B. Sabin* 1255
Plastic socket and lid reconstruction ..... *C. Parke Scarborough and Philip H. Landers* 1269
Presbyopia ..... *Lester L. Covell* 1275
Abducens paralysis in brucellosis ..... *Joseph C. Yaskin and Russell S. Boles* 1277
Organisms of the conjunctival sac ..... *Randolph W. Linhart* 1280
Lens changes in diabetes ..... *Winston Roberts* 1283
Subretinal hemorrhage ..... *Gyula Lugossy* 1285
Mercurialentis ..... *Emanuel Rosen* 1287
Conjunctival transplant for pterygium ..... *Janos Majoros* 1289
Correction in Prince's rule ..... *Malvin Proctor* 1289
Cosmetic cure of alternating squint ..... *C. Martin-Doyle* 1290
Streptomycin in conjunctival tuberculosis ..... *Peter Sykowski* 1291
A low-priced electromagnet ..... *I. Herbert Katz* 1292

DEPARTMENTS

Society Proceedings 1294
Editorials 1299
Obituaries 1303
Correspondence 1305
Book Reviews 1307
Abstracts 1311
News Items 1323

For complete table of contents see advertising page xi

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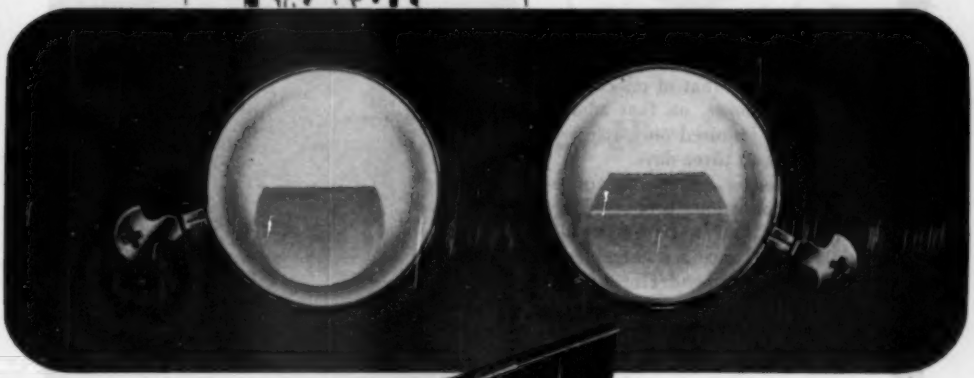

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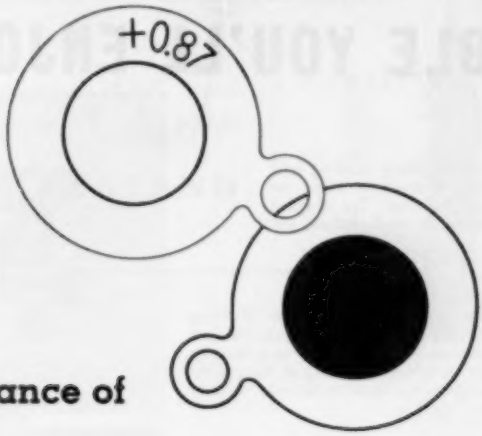

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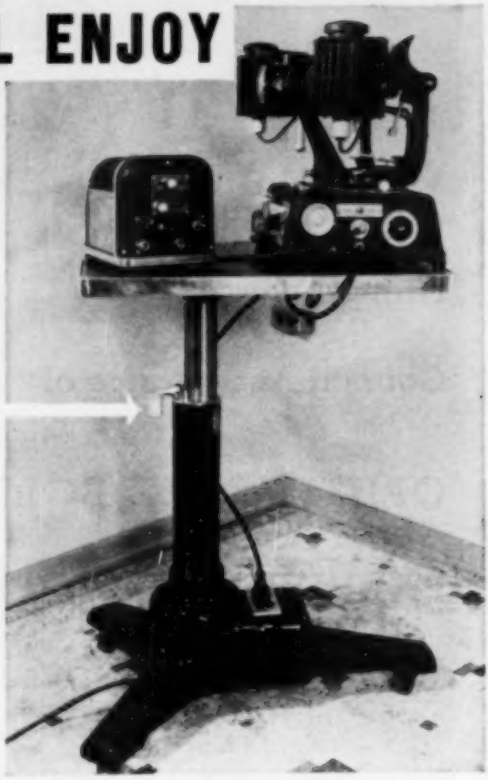

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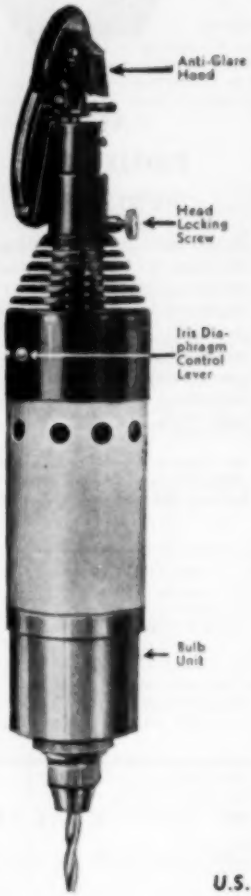

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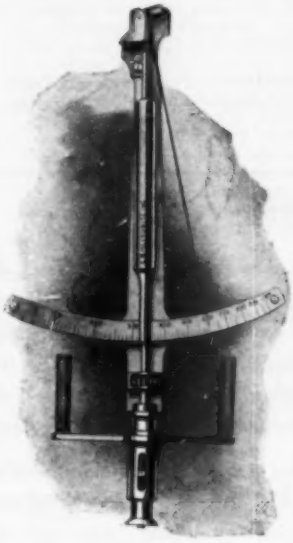

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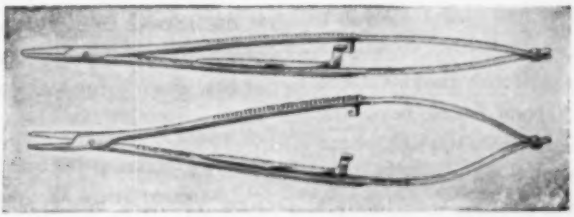

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The reason that myopic bifocals are troublesome lies in the fact that through the segments, even of the best available bifocals, base down prism is encountered. This base down prism makes objects appear farther away and higher than they really are.

The myope, before bifocals fixed his line of vision through a point 8 mm. below the distance center, invariably tipped his head and looked through a point near the distance center, thus avoiding prismatic effect. The hyperope on the other hand is not troubled by the base up prism he encounters and has little or no difficulty with bifocals.

From the foregoing it would seem that if the base down prism found in the segments of myopic bifocals could be neutralized, the problem would be solved. We have found this to be true. We have also found that the only practical way to accomplish this neutralization is by "slabbing off" the proper amount from the bifocal segments.

If we take a case requiring O.U.—6.00 with a +2.00 add made up in a small segment bifocal, we would "slabb off" 4.8 degrees of prism base up from both segments. ($6 \times .8 = 4.8$) that is, the distance correction through the 90th meridian times 8, the distance in cms. from the distance center to reading point, equals the amount of base down prism that must be neutralized.

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SERIES 3 · VOLUME 33 · NUMBER 8 · AUGUST, 1950

CONTENTS

ORIGINAL ARTICLES

Diabetic retinopathy. The Fourth Francis I. Proctor Lecture. Jonas S. Friedenwald. 1187
New procedure for the treatment of adherent leukomas preceding keratoplasty. Louis Paufique 1200
Epibulbar tumors. J. E. Ash 1203
Ewing's tumor of the orbit: Report of two cases. Fred Harbert and George L. Tabor, Jr. .. 1219
Streptothrix as a cause of follicular conjunctivitis and other obscure conjunctivitides. Frederick H. Theodore 1225
The effect of ACTH in glaucoma. Eugene M. Blake, Rocko M. Fasanella, and Andrew S. Wong 1231
Sutured contact lenses for contention of the graft in keratoplasty. Adrien Fritz 1236
Nondiabetic lipemia retinalis. Joseph J. Groom and C. Wilbur Rucker 1238
The effects of microwave diathermy on the eye: An experimental study. Louis Daily, Jr., Khalil G. Wakim, J. F. Herrick, Edith M. Parkhill, and William L. Benedict 1241
Toxoplasmosis: Diagnosis and treatment. Albert B. Sabin 1255
Plastic socket and lid reconstruction. C. Parke Scarborough and Philip H. Landers 1269
Presbyopia: Comparative observations of white and Negro populations. Lester L. Covell 1275
Abducens paralysis in brucellosis: Report of two cases. Joseph C. Yaskin and Russell S. Boles 1277
The effect of the eye patch on organisms of the conjunctival sac. Randolph W. Linhart 1280

NOTES, CASES, INSTRUMENTS

Rapid lens changes in diabetes mellitus. Winston Roberts 1283
Subretinal hemorrhage simulating sarcoma of the choroid. Gyula Lugossy 1285
Mercurialentis. Emanuel Rosen 1287
Conjunctival transplant for the treatment of pterygium. Janos Majoros 1289
Correction necessary in Prince's rule. Malvin Proctor 1289
Cosmetic cure of alternating squint. C. Martin-Doyle 1290
Streptomycin treatment of conjunctival tuberculosis. Peter Sykowski 1291
A low-priced electromagnet. I. Herbert Katz 1292

SOCIETY PROCEEDINGS

New York Society for Clinical Ophthalmology, November 7, 1949 1294
Memphis Society of Ophthalmology and Otolaryngology, August 13, 1949 1296

EDITORIALS

The June meetings 1299
Needless referrals 1302

OBITUARIES

Harry Searls Gradle 1303
Harry Friedenwald 1304

CORRESPONDENCE

Actions of extraocular muscles 1305
Clinical ophthalmic training in Alaska 1306

BOOK REVIEWS

Estrabismos y Paralisis 1307
Les Uvéites Hypertensives 1308
Transactions of the French Society of Ophthalmology 1309
Handbook of Physical Medicine and Rehabilitation 1310

ABSTRACTS

Anatomy, embryology, and comparative ophthalmology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy 1311

NEWS ITEMS 1323

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VOLUME 33 AUGUST, 1950 NUMBER 8

DIABETIC RETINOPATHY*

THE FOURTH FRANCIS I. PROCTOR LECTURE

JONAS S. FRIEDENWALD, M.D.
Baltimore, Maryland

With the general increase in life expectancy and in particular the increase in the life expectancy of diabetics, there has been an increase in the so-called degenerative complications of diabetes. The increased incidence of diabetic retinopathy in the past 20 years has been of truly alarming proportions. In my own private practice diabetic retinopathy is now three times as frequent as it was in 1924 when the incidence was the same as that in my father's practice in 1900. The incidence of cataracts and of glaucoma has not changed significantly in these same groups of patients.

A recent paper by Vogelius,[1] in which the frequency of diabetes and of diabetic retinopathy in Copenhagen is compared for the decades before and after 1937, indicates that in this community the frequency of retinopathy has increased very markedly in proportion to the number of diabetics, much more, in fact, than the increased survival time of diabetics would account for. Vogelius suggests that this increase may be attributable to the less rigid control of diabetes in the second period as compared with the first.

Evidence from other clinics, however, in which patients under rigorous control have been compared with patients under lax control, fails to support the notion that the degree of control of blood sugar has any significant direct effect on the incidence of the retinopathy.

Unless Vogelius's data are supported by studies from other clinics, one must keep in mind the possibility that the special stresses imposed on the Danish population during the war years may have something to do with the excessive incidence of diabetic retinopathy in the decade 1937-1947.

It may be helpful to review briefly the progress of our knowledge regarding this disease. For this purpose it is convenient to consider separately the pre-insulin and the insulin eras. Insulin was introduced in the early 1920's but it was not until the 1930's that enough young diabetics had survived long enough to alter significantly the statistical picture.

I. THE PRE-INSULIN ERA

The ophthalmoscopic characteristics of retinopathy in the diabetic were first systematically described and classified by Hirschberg.[2] In the interval between Hirschberg's report and 1930, discussion was chiefly focused on the question of the relation of the retinopathy to arteriosclerosis. The literature of this period has been well reviewed by Duke-Elder[3] in his textbook and only the arguments will be summarized here. Most observers promptly accepted the differences pointed out by Hirschberg between the diabetic and the nephritic retinopathies. The distinctions involve not merely the familiar differences in ophthalmoscopic patterns noted by Hirschberg, but also in the associated general clinical findings.

* From the Wilmer Ophthalmological Institute of The Johns Hopkins Hospital and University. Presented at the University of California Medical School, San Francisco, September 16, 1949.

The prognostic significance of the diabetic retinopathy for life expectancy is not nearly as ominous as that of the hypertensive or nephritic type. Many patients with diabetic retinopathy have normal blood pressure and normal renal function. Even when nephrosclerosis and hypertension supervene in the diabetic, the typical ophthalmoscopic picture of hypertensive retinopathy is rarely superimposed on that of diabetic retinopathy.

It is, no doubt, a sad commentary on the esteem with which our specialty is regarded by the internists, that this distinction between diabetic and hypertensive or nephritic retinopathy which we have regarded as well established for half a century, has not been universally appreciated by internists. The chief of one of our leading medical clinics, for instance, stated a year ago that he knew of no difference between the two conditions.

The debate among ophthalmologists in the pre-insulin period concerned the possible relation of diabetic retinopathy to that of senile arteriosclerosis. Those who believed that the retinopathy was a separate and distinctive disease emphasized the distinctive character of the ophthalmoscopic picture, the frequent absence of any visible sclerosis of the retinal arteries, and the absence, in many cases, of clinical evidence of arteriosclerosis disproportionate to the patient's age.

Those who believed that diabetic retinopathy was an arteriosclerotic manifestation pointed to the similarity in ophthalmoscopic picture between diabetic retinopathy and the lesions seen in some elderly arteriosclerotics without diabetes. In the latter, waxy exudates and small punctate hemorrhages may also be observed. They pointed to the fact that diabetic retinopathy was observed (in the pre-insulin era) almost exclusively in the arteriosclerotic decades, the patients in almost all of the cases being over 40 years of age at the time of onset of the retinopathy.[4]

Moreover, the early senescence and the marked predisposition of the diabetic to arteriosclerosis was well known. Not merely the frequency but also the pattern of distribution of the sclerotic process is influenced by diabetes—witness the high frequency of gangrene of the feet in diabetics.

While the weight of the argument in the pre-insulin era may appear to rest with those who considered this an arteriosclerotic manifestation, influenced in frequency and in pattern by the diabetic process, the retrospective examination of these arguments seriously undermines their validity.

It is remarkable that the argument on both sides was not buttressed by histologic studies of the affected retinas. Prior to 1925, very few eyes with diabetic retinopathy, uncomplicated by retinal detachment or by secondary glaucoma, had been examined histologically and, in these few, no special attention had been directed toward the retinal vessels.

In order to fill this gap in our information, I undertook many years ago to study in serial sections the retinal vascular trees of typical cases. Ten cases were examined and in five no lesions whatever were found in the retinal arteries.

It may be concluded, therefore, that the retinopathy is not a consequence of local arteriosclerosis. These findings are in sharp contrast with those in senile arteriosclerotic retinopathy in which organic changes in the retinal arteries are regularly found specifically in the vessels supplying the affected portion of the retina.

More recent studies, which will be reported in detail in this paper, have shown that the characteristic vascular lesion of diabetic retinopathy is the formation of small capillary aneurysms, that such aneurysms are not, or only very rarely, seen in other conditions, and that many of the so-called deep punctate hemorrhages in diabetic retinopathy are aneurysms, not hemorrhages.

This has bearing on the second issue in the pre-insulin argument—namely, the resemblance in ophthalmoscopic appearance between diabetic retinopathy and that seen

in some cases of senile arteriosclerosis.

It must be remembered in this connection that the pre-insulin period was also for the most part the period before blood chemistry investigations became a routine and reliable part of the clinical examination. The diagnosis of diabetes in this era rested on urine examination. An appreciable number of the cases which were at that time classified as nondiabetic would now be disclosed as mild diabetics with high renal glucose thresholds. The number of cases in which the ophthalmologist erroneously suspects diabetes on the basis of the retinal lesion is now very small indeed.

Even with modern diagnostic procedures an occasional puzzling case remains, but these residual puzzles constitute problems in differential diagnosis rather than evidence concerning the pathogenesis of diabetic retinopathy.

One clinical feature is extremely useful in the differential diagnosis. Since many of the deep retinal "petechia" of the diabetic are in fact aneurysms, they tend to persist for weeks and months. True extravasations of similar size are generally absorbed in a few days. Reëxamination of the diabetic after the lapse of a week or two will, therefore, reveal many of the same "petechia" that were present at the first examination.

Reëxamination of the nondiabetic arteriosclerotic who happens to have some deep petechial hemorrhages in the retina almost always leads to finding that the petechias originally present have disappeared. New ones may have formed in the interval, but not as a rule in the same places.

Using this criterion, I have in the past several years seen no single case in which the ophthalmoscopic diagnosis of presumed diabetic retinopathy was in contradiction with other clinical findings. This does not mean, of course, that my guess on the first examination was always correct.

There is no doubt that the diabetic is very commonly afflicted with arteriosclerosis and that he may have arteriosclerotic vascular accidents in the retina as well as in other organs. A systematic analysis of the relation between diabetes and arteriosclerosis is given in the book by Shields Warren on the pathology of diabetes.[5] Warren points out that the arterial lesion most commonly seen in the diabetic is atherosclerotic in type, and that Mönckeberg's sclerosis (calcification of the media) and hyalin degeneration of the arterioles (the characteristic lesion of malignant hypertension) are both rarely seen in the diabetic. Some atherosclerosis is to be found in almost every diabetic who has had diabetes for five years or more. From Warren's statistics it would appear that the small number of cases that escape arteriosclerosis is increasing since the use of insulin became established. It seems likely, therefore, that some aspect of the diabetic process that is favorably affected by insulin is responsible for the diabetic atherosclerosis. Warren suggests that the high blood lipid content of the uncontrolled diabetic may be the cause of the atherosclerosis.

There would appear to be no doubt that atherosclerosis is responsible for the high incidence of coronary occlusion, of gangrene, and of cerebral vascular accidents in the diabetic. There would appear to be, however, no direct relation between the retinopathy and the atherosclerosis.

II. After the introduction of insulin

With the introduction of insulin, survival of juvenile diabetics became possible, and it soon was apparent that diabetic retinopathy was a common complication in this group of cases. Perspicacious students realized that many basic facts were lacking in our knowledge of the natural history of this disease, that many basic misconceptions had been carried over from the preinsulin period. As a preliminary to any deeper understanding, statistical studies were in order, and a series of such contributions by different investigators has added greatly to our knowledge. The first and most comprehensive of these studies was conducted by Waite and Beetham[6]

on the clinical material made available to them chiefly by Joslin. The findings in the eyes of 2,002 diabetics were compared with those of 457 nondiabetics of comparable ages.

The chief findings of this study, confirmed and somewhat amplified by subsequent investigators, are the following:

The ophthalmoscopic features most characteristic of the diabetic are the presence of deep punctate "hemorrhages" and waxy exudates. The occurrence of this form of retinopathy is related to the duration rather than to the severity of the diabetes, being most common in diabetes of moderate severity. The frequency and progress of the retinopathy is little if at all affected by the rigorous control of the diabetes either by diet or by insulin. The average time between onset of the diabetes and onset of the retinopathy is somewhat longer (10 to 15 years) in juvenile diabetics than in the older age group (5 to 10 years).

In 25 percent of the cases of retinopathy there is no ophthalmoscopic evidence of retinal arteriosclerosis, and the frequency and severity of retinal arteriosclerosis is not significantly different in the diabetic with retinopathy from that in the nondiabetic of the same age. The same may be said of the blood pressure. Among patients who have had diabetes for over 15 years, 60 percent show deep retinal "hemorrhages"; 40 percent show waxy exudates.

Hanum[7] in his similar study placed particular emphasis on the type of diabetic retinopathy characterized by preretinal and vitreous hemorrhages. This rare and more severe form of the disease comes on after a somewhat longer incubation period and is often preceded by the milder form. The relation of this severe form to the severity of the diabetes, to the rigors of control by diet or insulin, to retinal and general arteriosclerosis, is the same as in the milder group. Most investigators have concluded that, since there is no evidence that insulin therapy does harm in relation to the retinopathy, it is wise to press rather than withhold insulin.

One feature which escapes such statistical studies, but which is of great importance in evaluating the influence of suggested therapy, is the tendency of the retinopathy to undergo periodic remissions and exacerbations. This can be seen most dramatically in the cases with vitreous hemorrhage which often show periods of marked temporary improvement, but can also be demonstrated in the milder cases, particularly if observations are checked by frequently repeated fundus photographs.

Such photographs bring out the point already alluded to that the same punctate red spot may be present in the retina for many months, eventually to be replaced by a whitish dot or more usually, to disappear altogether. The waxy exudates also persist for long periods and eventually disappear.

Thus, retinal lesions of one or both types may be continuously present, but when the older ones have been accounted for, it has been my experience that new lesions generally appear in sudden crops. The intermittency of these exacerbations and the intervening periods of slow repair suggest that some intercurrent and often episodic factor may play an important role in this disease. The same facts add very largely to the hazards of therapeutic trials, and require the evaulation of alleged therapy on a large statistical basis with adequate controls.

III. Capillary fragility

Hanum was the first to point out that patients with the severe form of diabetic retinopathy involving preretinal and vitreous hemorrhages show increased capillary fragility. His findings in this respect have been abundantly confirmed, though there is still much argument as to how the test of capillary fragility can be most reliably performed.

My own experience is that the simplest procedure, namely placing a blood-pressure cuff above the elbow with a pressure of

100 mm. Hg for five minutes, is most satisfactory.

This is somewhat in contrast with the findings of others in respect to tests for hemorrhagic purpura and scurvy. In both of these conditions the reliability of the test for capillary fragility has been found to be greatest if cyanosis and excessive venous stasis are avoided, either by using lower tourniquet pressures for longer times or by applying controlled suction to limited areas. While it is true, that anoxia and venous stasis produce hemorrhages in normal individuals and hence blur the difference between normal and purpuric cases, anoxia and stasis appear to aggravate markedly the capillary fragility in the cases of diabetic retinopathy and hence to enhance the reliability of the test in these cases.

When the tourniquet test is applied in the simple way outlined above, normal individuals rarely show more than 25 petechia in the forearm, and those showing over 50 petechia can be classified as abnormal. The dorsum of the hand, wrist, and fingers, and the finger webs should be inspected with particular care. The test should not be repeated on the same arm more often than every two weeks.

If this test is applied to the milder and more common type of diabetic retinopathy characterized by deep retinal petechia and waxy exudates, the results are less striking. On the average more petechia are produced in diabetics with this form of retinopathy than in diabetics without retinopathy. The latter do not differ from normal individuals of the same age groups. If the same case is followed with tests regularly repeated every two weeks for many months, the results are often found to fluctuate abruptly, and a fair though not absolute correlation can be established between the sudden appearance of fresh crops of lesions in the fundi and the increased response to the tourniquet test.

Phenomena of this type have led many clinicians to try out the effects of therapy with ascorbic acid, rutin, moccasin venom, and so forth. Optimistic reports have been issued by several investigators, but, I believe not enough attention has been given in the past to the normal intermittency of the disease. If ophthalmoscopic examinations are made sufficiently often and with sufficiently minute care, intermittent periods of improvement can be observed in almost every untreated case, and the occurrence of such improvements can give rise to false therapeutic hopes.

So far as my own experience goes, I have encountered only one case of diabetes complicated by scurvy. This case proved instructive in the field of social medicine if not in relation to the etiology of diabetic retinopathy. The patient was a woman, aged 50 years, who lived in very modest circumstances in a small town. She had a severe diabetes and a severe retinopathy, required over 50 units of insulin daily for the control of her diabetes, and was sent home with this prescribed dosage. She returned a month later with her diabetes under good control but the retinopathy much worse. She had bleeding spongy gums and other evidences of a moderately severe scurvy. It developed that the cost of the insulin had taken so much out of her weekly cash resources that she had been forced markedly to curtail her diet. The scurvy was rapidly controlled in the hospital but there was no corresponding improvement in the retinopathy.

In a series of cases that I have treated with rutin there has, in general, been an initial reduction in the findings on the tourniquet test. After some weeks, in spite of continued administration of rutin, the tourniquet test tends to run its usual fluctuating course. In some cases I have been impressed with the fact that, although the number of petechia produced by the tourniquet test is not very different on chronic rutin therapy, the size of the individual petechia appear to be reduced. I am not convinced that the course of the retinopathy is significantly affected by this drug.

IV. Capillary aneurysms and capillary hyalinization

A. Distribution, character, and frequency of the aneurysms

The sharply outlined globular character of the deep retinal petechia, and their extraordinary long persistence raises the question as to what surface delimits and protects

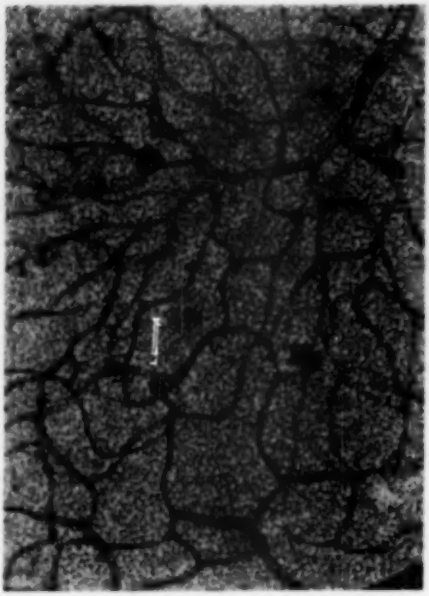

Fig. 1 (Friedenwald). Thin-walled capillary aneurysms. Flat preparation of a retina stained with the Hotchkiss-McManus stain.

these small pools of blood. Ballantyne and Loewenstein[8] were the first to find the explanation. By examining flat unstained unsectioned preparations of retina, they were able to show that in the diabetic retina most of what had previously been considered hemorrhages were not extravasations at all, but capillary aneurysms. They were unable to find similar capillary aneurysms in any other retinal disease.

The unstained preparations reveal very little more, since only the blood is clearly visible while tissue structures are but dimly seen. It was my good fortune to discover, in the course of some histochemical studies not directly related to the present problem, that the endothelium of the retinal vascular tree is surrounded by a basement membrane, one component of which is a mucoid or mucoprotein, stainable by the Hotchkiss-McManus[9] technique. The adaptation of this technique to flat preparations of unsectioned retina reveals most beautifully the whole retinal vascular tree. A preliminary report of the findings in diabetic retinopathy has already been published,[10] and a more extended analysis on the histochemical aspects has been reported by my collaborator, Dr. Robert Day.[10a]

Up to the present, the retinas of 76 cases of diabetes have been studied with this technique, and 43 of them show great numbers of capillary aneurysms, mainly in the region about the disc and macula. The average duration of the diabetes in the cases showing retinal aneurysms was 13 years, in the cases without retinal aneurysms five years.

A somewhat larger number of specimens from nondiabetics disclosed only one case in which there were an appreciable number of capillary aneurysms. This patient was a Negro, aged 57 years, who died on the surgical service from an inoperable carcinoma of the stomach. He had a hypochromic microcytic anemia. His fasting blood sugar was 100 mg. percent and his urine was sugar free. No sugar tolerance test was done.

Out of 13 cases of hypertensive retinopathy, three showed one or two isolated capillary aneurysms which were apparently related to some localized tissue injury. No capillary aneurysms were seen in the retinas of elderly arteriosclerotics without diabetes, with or without retinitis. It is to be concluded that the capillary injury which leads to aneurysm formation is not a manifestation either of atherosclerosis or of malignant hypertension and arteriolar hyalin degeneration.

Several of the cases of diabetic retinopathy showed localized retinal venous occlusions associated with abundant newly

formed capillary collaterals. The newly formed retinal capillaries, as has been pointed out previously, are distinguishable from the normal capillary bed by their irregular angular course and their irregular and often very wide diameters. Aneurysms are not seen in these newly formed vessels, consequently one can conclude that increased capillary pressure is not in itself sufficient to cause the aneurysmal dilatations. Some abnormal local weakness of the wall appears to be essential. Current studies indicate that aneurysms in the walls of venules and also, at times, in the capillary bed, are to be found in nondiabetic cases of retinal venous occlusion. The morphology of these aneurysms appears to differ from that of the diabetic capillary aneurysms.

In one of the cases of diabetic retinopathy that we have so far studied, there were, in addition to the newly formed intraretinal capillaries, also tufts of vessels extending into the vitreous. The terminal loops of these tufts showed bulbous ends resembling the intraretinal capillary aneurysms. Further study of the vascular pathology of retinitis proliferans seems indicated.

The intraretinal capillary aneurysms are mostly spherical in shape, 20 to 30 microns in diameter, and hence just at the limit of ophthalmoscopic visibility. Occasional larger ones up to 80 to 100 microns in diameter are to be found. Here and there one sees minute bulges in otherwise normal looking capillary walls which may represent beginning aneurysms, but these are so rare as to suggest that the aneurysms usually attain their globular shape at the very beginning of their development.

The most frequent location of the aneurysms is at the point of capillary bifurcation, in which case the aneurysm lies in the saddle between the two branches. The anatomic configuration here is similar to that of the congenital aneurysms that occur at the bifurcation of the large arteries at the base of the brain. Whether this localization is due to some local anatomic weakness or to hemodynamic factors is not clear.

A second point of predilection for the aneurysms is at sharp bends of the capillaries. Here the aneurysm forms on the outer, convex, surface of the bend. The aneurysms lie directly on the capillaries and are not attached to the vessel by a stalk. Consequently they must arise directly from

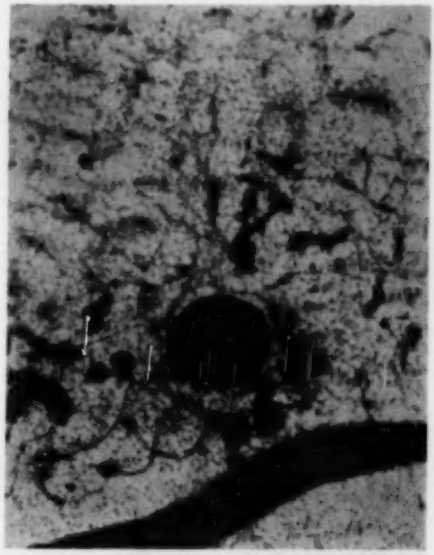

Fig. 2 (Friedenwald). Aneurysm with hyalinized wall surrounded by a cluster of exudates.

an outpouching of the vessel wall and not from the endothelization of a hemorrhage.

In unstained preparations the red blood cells within the aneurysms can usually be clearly seen. In the Hotchkiss stains the red blood cells are often obscured by the red color of the stained basement membrane. Ashton[11] has surmounted this technical difficulty by counter-staining the Hotchkiss treated retinas with benzidene which stains the red blood cells blue. The results of this combined staining technique leave no doubt whatever that the structures we have been calling aneurysms are true sacular aneurysms filled with blood and are not extravascular exudates.

While most of the aneurysms are globular, occasional cylindrical enlargements of a segment of capillary channel are to be seen. Also, occasionally adjacent globular aneurysms appear fused together in irregular patterns.

B. Relation to hemorrhages and exudates

Ballantyne was the first to note that true hemorrhages are not infrequently associated

Fig. 3 (Friedenwald). Globular and cylindrical aneurysms with hyalinized walls.

with the aneurysms. The occurrence of clusters of exudates about aneurysms was described in my previous communication and has been confirmed and amplified by Ashton. It is apparent that the location of the aneurysm must represent a weak spot in the wall of the capillary through which leakage of plasma proteins to form exudates and of red blood cells to form hemorrhages can readily occur. It is not clear whether the leakage occurs before or after the formation of the aneurysm. Some of the aneurysms which are surrounded by hemorrhages and exudates have particularly thick walls, suggesting either that the thickening of the wall may represent a reparative process tending to close the leak, or that the thickening may result from a deposit left in the wall during the leakage.

It is not to be concluded that exudates and hemorrhages are found only in the immediate environs of the aneurysms. Many are seen in regions where no abnormalities are visible in the capillary net. Presumably in these instances the lesion in the capillary wall is of submicroscopic dimensions or is healed without any structural residue.

C. Hyalin deposits in the capillary wall

Many of the aneurysms have markedly thickened walls. Some component of the material contributing to this thickening is a mucoid or mucoprotein which stains brilliantly with the Hotchkiss-McManus technique. It appears as a thickening of the basement membrane normally present, and like the basement membrane lies immediately beneath the endothelium. In routine sections stained with hematoxylin and eosin it has the appearance of hyalin. Often the hyalin deposit has a definitely lamellar structure. This can best be seen with silver stains, as Ashton has shown, and suggests that it is laid down in successive episodes. Sometimes the whole aneurysmal sac is obliterated by this hyalin material. Sometimes the aneurysms have, in addition to the hyalin, a thin outer covering of nonhyalin fibrous material.

I have occasionally noted on repeated ophthalmoscopic examination that a capillary aneurysm becomes converted into a sharply outlined white spot and presume that this is the ophthalmoscopic appearance of such a hyalinized aneurysm. More often the aneurysms disappear from the ophthalmoscopic picture without visible residue. This need not mean that such healed aneurysms are not hyalinized for the hyalin, if reasonably homogeneous, would not, as a general

rule, be ophthalmoscopically visible.

Hyalin thickening of the basement membrane is most prominent in the aneurysmal wall but, in severe cases of retinopathy, similar thickenings may be seen in the walls of capillaries with quite normal appearing internal channels.

Sometimes these hyalin deposits are lumpy suggesting that they may be the residue of old obliterated and partially reabsorbed aneurysms, but often they form a smooth cylindrical coat which appears to be quite unrelated to aneurysm formation. One is forced to the conclusion that even if the capillary aneurysms and the hyalin thickening of the capillary basement membrane are both consequences of the same metabolic disturbance, their local development must be to some degree independent. Aneurysms exist in which the wall is no thicker than that of a normal capillary, and hyalin thickening of the basement membrane can occur where there are no aneurysms.

D. Related Changes in Other Organs

Having become familiar with some aspects of the capillary lesion which characterizes the diabetic retinopathy, it is only natural to inquire whether similar vascular changes are to be found in other organs. The scanty harvest that can be reported from this field should not be taken as final for the retina is remarkably suited to the techniques so far applied. Its thin structure makes possible the study of its vascular tree without sectioning. In most other organs the capillaries form nets, the individual threads of which are generally 100 or more microns apart. Preparations that are thick enough to reveal the vascular tree are usually too opaque for satisfactory study. On the other hand, if a capillary aneurysm happens to be cut in an ordinary thin section it can rarely be distinguished from a normal or a hyalinized venule. Reconstruction in serial sections is an extremely laborious undertaking, to be avoided until all other possible approaches have been exhausted.

Ashton reports that he has been unable to find microaneurysms in the ocular tissues other than the retina and my own efforts with respect to the intraocular tissues have been similarly unrewarding. The series which I have studied has included three cases of rubeosis of the iris. The latter, however, deserve much more study than has so far been given them.

Dr. Day and I, using the corneal microscope, have studied the conjunctival vessels of 60 successive cases of diabetic retinopathy. In only one was a single capillary aneurysm found. Since such aneurysms are occasionally to be seen in nondiabetics, no significance is to be attached to this finding.

Fig. 4 (Friedenwald). Hyalinized capillary aneurysms. Note that the globular nodule at (A) surrounds a capillary channel of normal dimensions. Hyalinized capillary without aneurysm at (B).

In 40 cases of diabetic retinopathy the capillary loops at the fingernail bed were also studied with the corneal microscope, and in three cases clusters of capillary aneurysms were found. It is very difficult to exclude trauma in relation to these lesions but no

similar lesions have as yet been found in a comparable group of nondiabetic controls.

Tourniquet tests were applied to these cases and the capillary aneurysms were watched during the test. No fresh aneurysms in the fingernail bed appeared during the five-minute application of the tourniquet at 100-mm. Hg pressure, and the aneurysms though distended did not rupture.

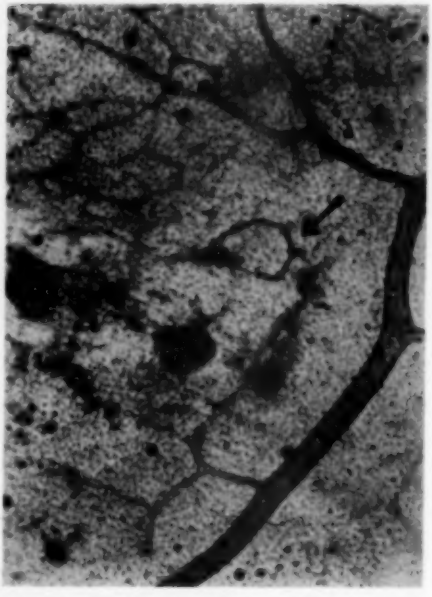

Fig. 5 (Friedenwald). Two hyalinized aneurysms each surrounded by a thin outer wall that stains feebly with the Hotchkiss stain. The arrow indicates a capillary with hyalinized wall without aneurysms.

I am reporting these incomplete data at the present time not because I believe any special significance should be attached to them, but in the hope of stimulating others toward a similar search. If it should prove possible to attribute these lesions to the diabetic process, they may serve as suitable test objects for a study of the pathologic physiology of the condition.

Capillary aneurysms were searched for in the brains of 10 cases of diabetic retinopathy available for post-mortem study. Sections of the tissue were cut 50 microns thick and stained with the Hotchkiss-McManus technique. One capillary aneurysm was found.

E. Relation to renal lesions

Kimmelstiel and Wilson[12] were the first to discover in kidneys of long-standing diabetics a peculiar lesion to which they gave the name "intercapillary glomerulosclerosis." The lesion is characterized by the presence of globular hyalin nodules, usually situated near the periphery of the glomerular tuft, by irregular strands of similar hyalin material between and surrounding the glomerular capillaries, and, as Allen[13] pointed out, by the presence of enlarged or dilated capillaries in glomeruli.

Studies by many pathologists have led to the conclusion that the globular hyalin nodules are the most characteristic aspect of the lesion. They are found in appreciable frequency in long-standing diabetics, only with the greatest rarity in other conditions. The irregular strands of hyalin, on the other hand, are commonly seen in various nondiabetic types of nephrosclerosis. The diagnosis of the diabetic nephropathy is now generally limited to those cases showing the globular lesions.

Wagener[14] and others have reported studies correlating antemortal ophthalmoscopic examination with postmortal examination of the kidneys. They found that 80 to 90 percent of the patients having the diabetic nephropathy also had the diabetic retinopathy. About half of the cases with clinically recognizable diabetic retinopathy are found at autopsy to have diabetic nephropathy. The frequency of both lesions increases with the age of the patient and increases much more markedly with the duration of the diabetes. It is to be concluded that these two conditions are closely related, but questions remain as to the identity of the pathogenetic mechanisms involved.

Dr. Day, who studied the material avail-

able in the department of pathology at the Johns Hopkins Hospital, found that, out of 43 diabetics with retinal capillary aneurysms, 25 showed typical nodular hyalin deposits in their renal glomeruli, while out of 33 diabetics with no retinal capillary aneurysms, none showed the characteristic renal lesion. Ashton has reported similar incidence in a smaller series. Out of 21 diabetics studied by him, 12 showed capillary aneurysms in their retinas and, of these 12, seven were found to have the characteristic renal lesion. None of the nine without retinopathy showed the characteristic nephropathy.

It should be pointed out that in both of these studies the whole retinas were examined in flat preparations while only a few sections of the kidneys were studied. The criteria for the diagnosis of the renal lesion were, therefore, more severe than for the diagnosis of the retinal lesion. Some of the milder cases of nephropathy in which no globular nodule happened to be present in those glomeruli that were studied were classified as free from the renal lesion.

It does not follow from these data, therefore, that the retinopathy necessarily precedes the nephropathy, or that the retinopathy can be present when the renal lesion is totally absent. Ashton has pointed out that there is no exact correlation between the severity of the retinal and renal lesions. Nevertheless these data do show that the correlation between retinal and renal lesions is even closer than had been found previously.

The hyalin material in the renal glomeruli is found in or on the capillary basement membrane. Kimmelstiel and Wilson believe that it is deposited in the intercapillary connective tissue, while Allen states that the hyalin, though subendothelial, is within the vessel wall. This difference of opinion can hardly be resolved with presently available techniques.

Since the staining characteristics of the hyalin are similar to those of the capillary basement membrane, one cannot say with assurance whether the hyalin is bounded on its outer or inner surface by the basement membrane, or whether the membrane is spread apart and infiltrated by the hyalin, but all are at least agreed that the hyalin is contiguous with the membrane. The same can be said of the location of the hyalin in relation to the walls of the retinal capillaries and capillary aneurysms.

Ashton has made extensive comparisons of the staining characteristics of the retinal and glomerular hyalin and concludes that the two materials are strikingly similar. I agree with this so far as the hyalin deposit in the capillary and aneurysmal walls are concerned. The associated waxy exudates which lie in the outer fibrillar layer of the retina and are not directly in contact with the vessel walls do not seem to me to be identical with the capillary hyalin.

With the Hotchkiss stain these exudates show, in general, a much less intense color than does the capillary hyalin, often no more intense than the blood serum within the vessels. They are usually quite homogeneous and even when showing fine cracks and irregularities rarely give the concentric lamellation of the capillary hyalin or of those solid round nodules attached to capillaries which, I have suggested, may represent filled and occluded aneurysms.

If one wishes to press the histologic analogies as far as possible, it is these occluded aneurysms rather than the waxy exudates that most closely resemble the glomerular nodules. I have, however, so far not seen a glomerular nodule with a central hollow such as is so characteristic of many of the retinal capillary aneurysms.

A further possible analogy between the two lesions concerns the dilated capillaries first noted in the glomeruli by Allen. In a previous paper I have suggested that these may in fact be thin-walled capillary aneurysms. Ashton has criticized this suggestion. The hyalin nodules might, as he correctly points out, distort and compress some of

the glomerular capillaries and through stasis cause their passive dilatation. The capillary dilatations, however, do not always occur in the same glomeruli as the hyalin nodules. They are usually located centrally in the glomerular tuft while the hyalin nodules are usually peripheral. Occasionally their walls are hyalinized.

In summary the hyalin material lying in or on the capillary walls in the retina and in the renal glomeruli appears to be identical, but there is no certain retinal analogue for the nodular form of the hyalin deposits in the glomeruli, though these may represent occluded capillary aneurysms, and there is no certain renal analogue for the retinal capillary aneurysms, though the dilated capillaries described by Allen may be aneurysmal.

It is, I believe, worth while to push the analysis of these analogies as far as possible, since the wider the analogies the firmer would be the conclusion that the two lesions are manifestations of the same disease process. Even if this conclusion is true, and I believe the weight of evidence in its favor is now great, one would expect at some point in the analysis to encounter discrepancies, in view of the enormous functional and morphologic differences between these two sets of capillaries. The extent of the analogy between the retinal and glomerular lesions is all the more surprising in view of the paucity of the present evidence in regard to related lesions in other organs.

Discussion

In a field in which knowledge is advancing as rapidly and as unexpectedly as this one, it is hazardous to stake out too many conclusions. Nevertheless there are some conclusions which can be drawn with a high degree of assurance, and some opinions which, with due reserve, it seems worthwhile to hazard.

The chief conclusions are that diabetic retinopathy is not an atherosclerotic manifestation, that the vascular lesion which results in the retinopathy is specifically related to the diabetes, that the renal lesion described by Kimmelstiel and Wilson is a very closely related condition. I do not believe that other organs have as yet been adequately explored, by adequate techniques, to disclose the full extent of this vascular disturbance.

These conclusions justify the search for some metabolic disturbance of the diabetic which is specifically related to the vascular lesion. It is clear that the retinopathy bears no direct relation to the blood sugar, but we have already advanced far from the naïve idea that diabetes is merely hypoinsulinism. There is, for instance, good experimental evidence that partial pancreatectomy produces a more severe disturbance of carbohydrate metabolism than does complete pancreatectomy. The implication that there may be a hyperglycemic factor in the pancreas, an antagonist to insulin, has received some experimental support. The work of the Cori and their co-workers[15] has greatly clarified an antagonism between the pituitary and the pancreas. In view of this, the complete normalization of the blood sugar by insulin injections cannot be supposed completely to normalize the diabetic.

Chaikoff and Entenman[16] have recently reviewed the present knowledge dealing with the antifatty-liver factor of the pancreas. There appears to be no direct connection between this factor and the diabetic process, but there are still sufficient uncertainties to justify keeping an open mind about a possible connection.

McManus[17] has recently suggested that the source of the hyalin material which is deposited in the glomeruli may be a polysaccharide present in the blood of the diabetic in abnormal concentration. In fact, Jacobs[18] has demonstrated a mucopolysaccharide in the blood serum of diabetics, and has shown that the concentration of this polysaccharide closely parallels that of the blood glucose in response to insulin.

It may not be too far-fetched to point out

that there is an increase in the mucopolysaccharide content of the serum also in some chronic infections in which amyloidosis is a not infrequent complication. The amyloid material which is deposited in amyloidosis is certainly different from that which is a component of the hyalin deposits in the diabetic, but the amyloid material is, in part, also deposited in the blood vessel walls.

Most recently there has appeared a report by Pirani[19] on the occurrence of amyloidosis in chronic experimental scurvy in guinea pigs. If this is confirmed, we shall have further evidence of the possible relation of capillary fragility to a disturbance of the polysaccharide metabolism. These suggestions are indeed tenuous, but they justify the demand for a much more extended analysis of mucopolysaccharide metabolism in relation to diabetes and diabetic retinopathy.

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NEW PROCEDURE FOR THE TREATMENT OF ADHERENT LEUKOMAS PRECEDING KERATOPLASTY

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The surgical treatment of adherent leukomas has always been considered a difficult and delicate operation, likely to be accompanied by various complications.

Before the present practice of corneal grafting, there were two chief indications for operation. The first was to restore a certain degree of vision by means of iridectomy, so-called optic; the second to combat the most dangerous complication of adherent leukomas, secondly optic hypertension which might lead to the formation of anterior staphyloma and, especially if of long duration, cause a definite impairment of visual function.

The first operation, that most generally employed, optic iridectomy, presents no technical difficulty and, as a rule, is not followed by complications. There is genuine improvement of visual acuity, although often limited to 1/20 to 1/10, for reasons which have been noted in the chapter on "indications" in my report on keratoplasty.

In large adherent leukomas, however, iridectomy is usually not effective in preventing ocular hypertension and its resultant complications. Then the various classical procedures are all difficult, often dangerous or ineffective. Simple section with a Graefe knife introduced into the anterior chamber usually fails, because the elastic iris is drawn in by the instruments and the section is badly done. A large piece of iris remains attached to the posterior surface of the cornea and often new anterior synechias reform.

If we try, after corneal sutures at the limbus, to grasp the adherent iris with a forceps-scissors we find that the maneuver is very difficult after evacuation of the aqueous humor and there is grave risk of provoking a traumatic cataract or an attack of glaucoma.

Keratoplasty, so often indicated in the numerous forms of adherent leukoma, seemed at first the ideal operation, since it permitted the excision of the entire leukomatous disc by resecting the iris at a distance all around the affected zone with the trephine and replacement of the diseased cornea by a healthy graft capable of reestablishing transparency.

I have done four corneal grafts for this indication. The results were unsatisfactory.

In the first case, I provoked a traumatic cataract by trying to withdraw a segment of iris with a Hess forceps.

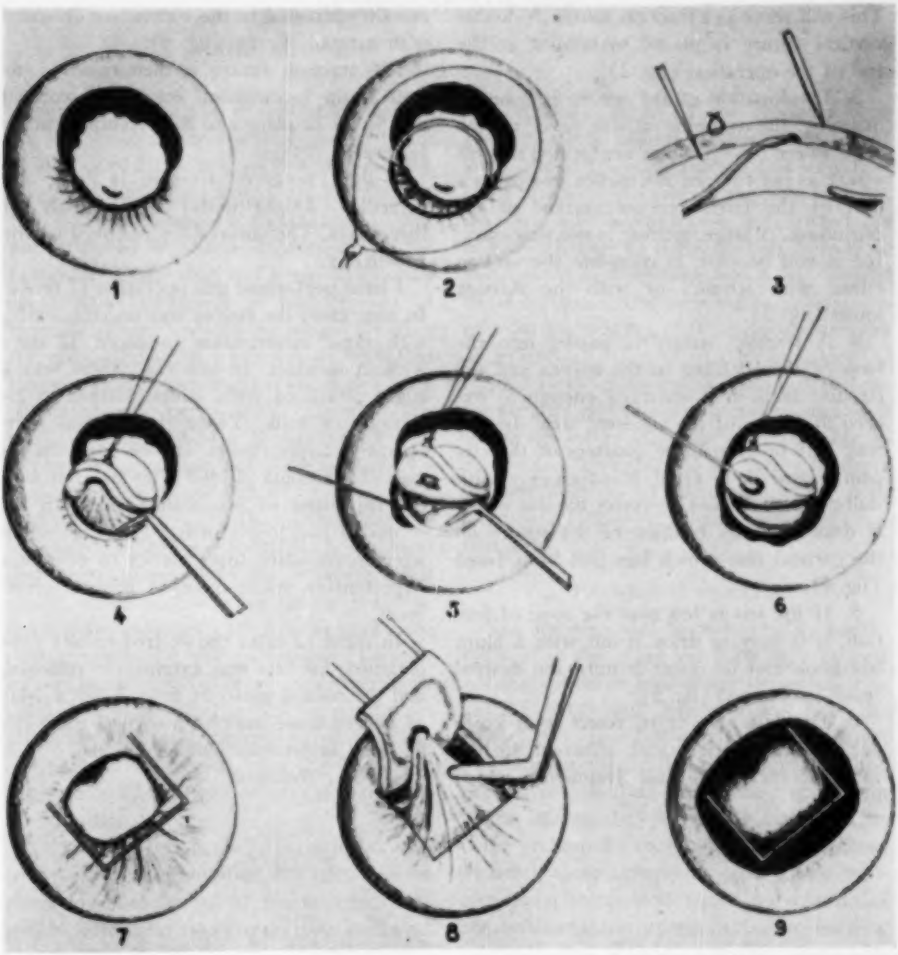
In the second case, the operation was followed by an attack of diffuse keratitis with secondary hypertension, and ectasia of the graft which became opaque and highly vascularized.

In the third case, also followed by a violent glaucomatous reaction, the graft was eliminated at the end of the month by a slow necrosis.

Finally, in the last case, in which the postoperative course was remarkably smooth, the graft became opaque and another keratoplasty was necessary.

I, therefore, sought a means of preventing these dangerous complications and invented a method of treating these corneal leukomas, preparatory to corneal grafts.

The main idea is that we must utilize penetrating keratoplasy which permits perfect access to the posterior surface of the diseased cornea and resection of the adherent iris. But, instead of placing a graft, we replace the diseased cornea thus liberated and this autograft, so to speak, has every chance of being well tolerated. It is rapidly reunited to its original primary bed and does not run the risk of being impaired by the postoperative complications which may ensue in a certain number of cases.



Figs. 1 to 9 (Paufique). Steps in technique for surgical treatment of adherent leukomas preceding keratoplasty. (1) A leukoma with considerable iris adhesion. (2) Placing of the traction suture. (3) The section is completed with scissors or the Arruga forceps. (4 and 5) Resection of the iris. (6) Iris fragments remaining on cornea are removed with a small curette. (7 to 9) Variation in the procedure shown in Figures 1 to 6, using the square incision.

The method should be employed in all cases where there is a leukoma with considerable iris adhesion (fig. 1). Only thin synechias which are isolated or peripheral can be treated by simple section or iridectomy.

The different stages of the procedure are as follows:

1. I begin by marking with a slight pressure of the trephine the site of trephination on the cornea. It should exceed by about two mm. the corneal implantation of the anterior synechias. I generally use a six-mm. trephine.

2. I place on the edge of the corneal disc thus outlined a loop of knotted thread.

This will serve as a traction suture. A double vertical suture is placed to hold it at the end of the operation (fig. 2).

3. Trephination of the cornea is done by inclining the trephine at the level of the edge where the synechias are located in such a way as not to open the cornea except on a part of the circumference marked at the beginning. A large opening is not necessary, for it will be easy to complete the section either with scissors or with the Arruga knife (fig. 3).

4. A traction suture is passed into the loop of thread fixed in the cornea and the circular incision is enlarged enough to exceed the limits of the adherent zone. In this way half or even three quarters of the circumference can be freed. It is then easy, with dull-pointed scissors, to resect the iris which is drawn out by traction of the suture on the corneal disc which has just been freed (fig. 4).

5. If the iris is too near the zone of section, it is easy to draw it out with a blunt iris hook and to resect it until the desired result is obtained (fig. 5).

6. The last step is to resect with knife or scissors the iris still adherent to the raised cornea. The last fragments which remain encrusted in the cornea are detached with a small curette (fig. 6).

The traction suture is then removed, as well as the intracorneal suture, the corneal disc is set in place and the retention suture fastened.

A light pressure dressing is used, and penicillin (200,000 units) is given daily for three days. The sutures are removed on the fourth day.

I have performed this operation 12 times: In nine cases the course was uncomplicated, with rapid cicatrization in about 12 days without incident. In one case, there was a slight attack of iritis which yielded to injections of milk. Twice, I observed postoperative hypertension. In one case, the attack of glaucoma yielded after two retrobulbar injections of scurocain-alcohol. In the second, I had to perform a Lagrange iridosclerectomy after three weeks to overcome hypertension which resisted medical treatment.

In these 12 cases the desired results were obtained, the iris was extensively removed, and the cornea perfectly free. After a delay of two or three months, a corneal graft can be done under excellent conditions.

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EPIBULBAR TUMORS*

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Several years ago a review of the epithelial tumors of the limbus was made with the assistance of Helenor Campbell Wilder[1] and, about the same time, a study of conjunctival nevi and melanomas was carried out but was not published. We were impressed with the favorable results that had been obtained by conservative treatment in both groups of lesions and ever since we have been pleading for conservatism in treatment of epibulbar tumors. This presentation is taken as an opportunity to bring to wider attention this thesis, particularly as it is substantiated by a much larger amount of material and by a more extended follow-up.

We have received at the Institute several eyes that had been enucleated for benign nevi and other lesions which our experience has shown to be amenable to simple excision. Even more frequently the lesions have been misinterpreted by the pathologist, particularly if he has not had much experience with ophthalmic material. This has occurred most commonly with the benign nevus and the conjunctival lymphoma, for the histologic appearance of both can be very deceiving to the uninitiated.

The title of this paper is all-inclusive but, while a certain amount of attention will be given to other epibulbar lesions, emphasis will be placed on two groups: the epithelial changes and the melanomas including nevi. As a matter of fact, there is little to be gained from a detailed morphologic and statistical review of such lesions as dermoids, pterygia, and pingueculas, and the rarer vascular tumors.

A special analysis of our group of lymphomas will be included. With its absence of well-defined follicular pattern and its apparent infiltration of covering mucosa, lymphoma is not infrequently interpreted as lymphosarcoma. In our collection there is no instance of a lymphoma which has proved to be malignant clinically unless it was part of systemic disease, that is, lymphosarcoma or leukemia.

This report is based on the clinical data, the surgical and autopsy specimens, and such follow-up information as were available in 1,120 cases in the files of the Army Institute of Pathology as of December, 1946, with additional follow-up material received since that date.

Pathologic criteria

The statistics will be more readily understood if at this point the pathologic criteria for the epithelial lesions are presented. Excluding congenital dermoids and nevi the epithelial lesions fall into three categories:

1. Epidermidalization or metaplasia of the normal conjunctival and corneal epithelium to the squamous type (figs. 1 and 2). This is the preliminary change to the development of other more serious lesions. It is a very common phenomenon which may occur in any inflammatory process in the conjunctiva, just as it does in other mucosae which take origin from the ectoderm.

This altered epithelium may undergo one of three further changes:

a. Dyskeratosis (included in Group 1), which in turn may be either of two types: (1) Leukoplakia, which is much the commoner (fig. 3). (2) Bowen type 2, such as is seen in the classic dermatosis of that name (fig. 4).

2. Papilloma formation (figs. 5 and 6).

3. Frank squamous or basal-cell carinoma which may develop from either the leuko-

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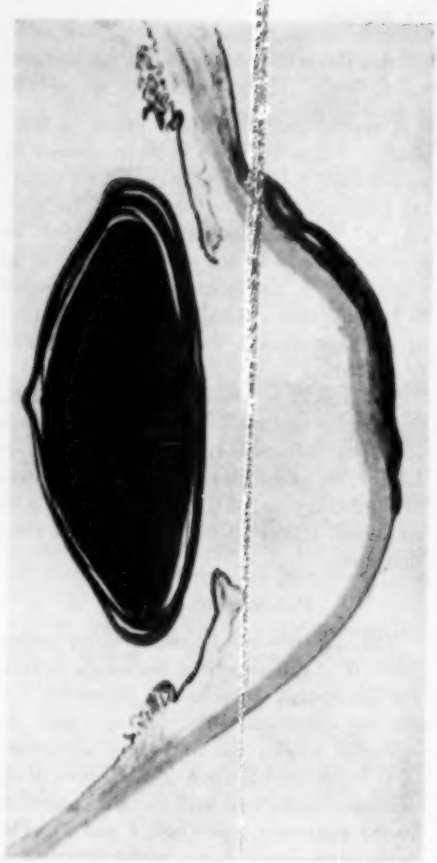

Fig. 1 (Ash). Epidermidalization of corneal epithelium. (AIP Neg. 72104.)

plakic dyskeratosis, or from the secondary papillomatous tissue (fig. 7).

Fortunately, the epithelial lesions on the cornea are frequently superficial and may be stripped off without disturbing Bowman's membrane. Occasionally, however, carcinoma developing in the altered epithelium may penetrate the sclera and infiltrate the intraocular structures (fig. 8). In our material there is but one instance of carcinoma developing in the 19 cases of pure Bowen type of dyskeratosis, and there are 53 instances of the basal-cell type of carcinoma, approximately half of them in the inner canthus.

General clinical statistics

Before referring briefly to the general clinical statistics derived from the whole group, it is necessary to call your attention to the fact that from a purely statistical standpoint our figures for the distribution of the various lesions by sex and age are not representative of the distribution in the general population. Of the 1,120 cases, 400 are from Army personnel on active duty during World War II and, therefore, are

Fig. 2 (Ash). Diffuse papillomatosis at limbus epidermidalization of corneal epithelium. Compare with intact conjunctival epithelium at both sides. (AIP Neg. 72106.)

predominantly male and from the relatively fixed military age group which is arbitrarily placed at 18 to 40 years.

The 720 cases that have been submitted to the American Registry of Pathology by

Fig. 3 (Ash). Epidermidalization at limbus, leukoplakic type of dyskeratosis. Marked inflammatory reaction. (AIP Neg. 72086.)

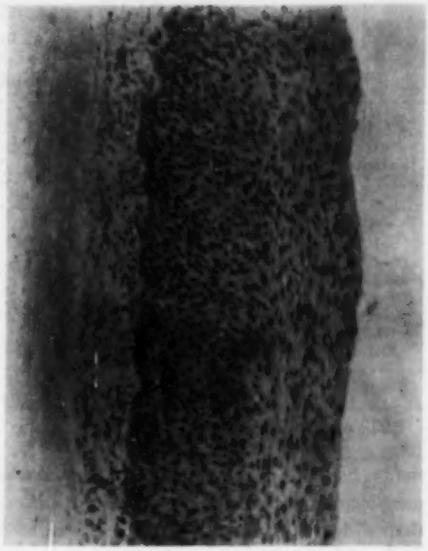

Fig 4 (Ash). Epidermidalization at limbus, Bowen-type dyskeratosis. Comparative lack of inflammatory reaction. (AIP Neg. 72109.)

civilian ophthalmologists more nearly represent the normal age and sex distribution, but they are not fully representative as to types of lesions since, in general, men of military age with benign lesions were acceptable for service in the armed forces while those with malignant lesions remained in the civilian group.

The Army cases influence in slighter degree the figures as to racial distribution. Race was recorded for 80 percent of the patients, among whom 90 percent were white, and 9 percent were Negro. The remaining one percent were members of other races.

The proportion of Negroes in this series approximates that of the Negroes in the total population of the United States (10 percent). As Table 1 shows, the Negro pa-

TABLE 1

NUMBER AND RELATIVE PERCENTAGES OF SPECIFIC EPIBULBAR LESIONS BY RACE

Pathologic Diagnosis*	Number		Percent	
	White	Negro	White	Negro
Epithelial tumors	311	35	35.5	39.8
Nevus	277	17	31.7	19.3
Malignant melanoma	57	3	6.5	3.4
Dermoid and teratoma	63	6	7.2	6.8
Other benign neoplasms†	26	1	3.0	1.1
Pterygium and pinguecula	72	17	8.2	19.3
Other‡	69	9	7.9	10.3
Total with race known	875	88	100.0	100.0

* This table represents only one pathologic diagnosis for each patient; in cases with more than one diagnosis, the more malignant lesion was counted.

† Includes lymphoma and vascular tumors.

‡ Includes such rare diseases as xeroderma pigmentosum.

TABLE 2

DISTRIBUTION OF EPIBULBAR LESIONS BY AGE*

Age of Patient	Diagnosis									
	Epidermidalization	Papilloma	Carcinoma	Pterygium & Pinguecula	Misc. benign Neoplasms	Teratoma, Dermoid & Der. Cyst	Nevus	Malignant Melanoma	All Other Lesions	Total
10	1	9	0	0	10	25	14	0	11	70
10–19	3	4	3	8	9	24	38	3	12	104
20–29	8	37	11	32	16	21	137	3	26	291
30–39	11	29	29	22	10	3	41	12	14	171
40–49	9	14	16	10	10	2	14	9	8	92
50–59	13	15	37	15	2	—	8	12	9	113
60–69	13	11	39	5	3	—	6	12	10	99
70+	8	7	37	3	3	—	1	14	3	76
Total	68	126	172	95	63	75	259	65	93	1016

* The age of 104 patients is not known.

tients had significantly more pterygia and pingueculas and fewer melanomas and nevi than did the white. The striking differential in incidence of pigmented tumors between white and black patients is a repetition of our experience with the intraocular melanomas; in that series only 8 out of 1,600 were from Negroes.

The influence of the Army collection is evidenced in the age distribution. In the 1,016 cases in which age is recorded, nearly one half were between the ages of 18 and

Fig. 5 (Ash). Papillomatosis at limbus, histologically early squamous-cell carcinoma. Marked epidermidalization of corneal epithelium. (AIP Neg. 72108.)

Fig. 6 (Ash). Massive papillomatosis at limbus and over cornea, histologically early squamous-cell carcinoma. Epidermidalization of conjunctiva at top. (AIP Neg. 72112.)

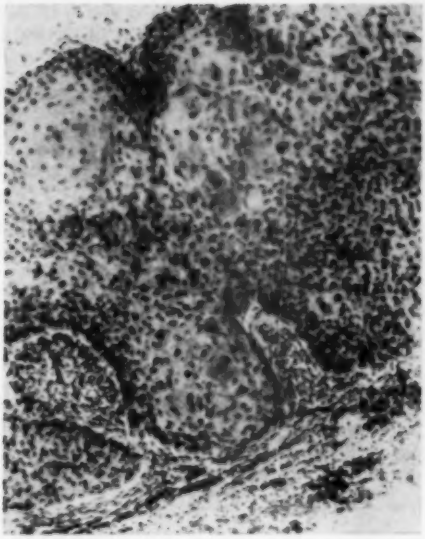

Fig. 7 (Ash). Papillomatosis showing leukoplakic type of malignant dykeratosis, "carcinoma in situ." (AIP Neg. 63167.)

Fig. 8 (Ash). Penetration of sclera and invasion of ciliary body by squamous-cell carcinoma primary in limbal conjunctiva. An infrequent complication (AIP Neg. 66879.)

39 years. In the entire series, however, the youngest patient was one year old and the oldest 97 years.

Table 2 shows the distribution of the various pathologic categories by age. The percentages are shown graphically in Chart 1. The age distribution of the patients with the

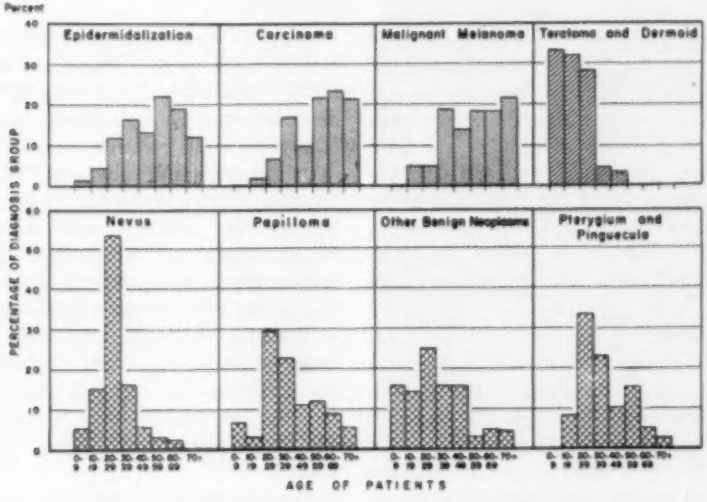

Chart 1 (Ash). Relative frequency of specified lesions by age group.

lesions observed is in great part dependent on the age distribution of the population from which they are drawn; and except for a general knowledge of the age of the military group, this is unknown. The various lesions, therefore, can be compared among themselves with respect to age distribution but not with those drawn from other populations.

The age distribution graphically presented in Chart 1 is what might be expected from the nature of the lesions. The malignant tumors gradually increase in frequency in the early decades and reach a sustained high plateau in the last 3 or 4 decades, with little or no decrease in the older ages. Teratomas and dermoids, on the other hand, are most frequent early in life and rare in the older age groups. Between these two are the benign neoplasms and the inflammatory lesions, such as pterygium, papilloma, nevus, lymphoma, which rise to a peak in young adults and generally decline with increasing age.

The incidence of any of the tumors is apt to be relatively higher in members of the military group because they are under constant medical supervision, and, in them, lesions for which the civilian patient would probably not seek medical care are brought to light and treated. This factor strongly influences the statistics covering the duration of the various lesions as well as the age distribution.

Sex. Eight hundred, or 71 percent, of 1,120 epibulbar lesions were in males; 26 percent in females. The attempt was made to determine, as far as possible, the influence of sex on the development of various lesions as summarized in Table 3. Among both the civilian and the Army personnel there were significantly more males who received treatment for such lesions as epidermidalization and carcinoma.

TABLE 3

DISTRIBUTION OF EPIBULBAR LESIONS BY SEX*

Pathologic Diagnosis	Number		Percent	
	Male	Female	Male	Female
Epidermidalization	64	6	8.0	2.1
Papilloma	102	29	12.8	9.9
Squamous-cell carcinoma	116	20	14.5	6.9
Basal-cell carcinoma	38	8	4.8	2.7
Nevus	241	84	30.1	28.8
Malignant melanoma	36	31	4.5	10.5
Dermoid and teratoma	45	33	5.6	11.3
Other benign neoplasms	22	16	2.7	5.5
Pterygium and pinguecula	70	35	8.7	12.0
Other lesions	66	30	8.3	10.3
Total with sex known	800	292	100.0	100.0

* No statement as to sex was made in the records of 28 patients.

Since the entire series is weighted on the side of males by the inclusion of Army material, a separate analysis of the 615 civilians disclosed that a significantly higher percentage of males received treatment for epidermidalization and carcinoma; while a significantly higher percentage of females were treated for dermoids and miscellaneous benign neoplasms. A possible explanation for the higher percentage of material representing the more serious lesions among males is that the diagnosis was made by local board physicians or Army medical examiners at the time the men appeared for induction through the Selective Service System, and the necessity for treatment was emphasized.

Sites of various lesions. A summary of the

locations of the lesions under consideration is presented in Table 4. The largest number was concentrated on the conjunctiva as exposed through the palpebral fissures, emphasizing the role of chronic irritations in their production. It is interesting to note that the papilloma is a common lesion of the caruncle. The fact that it is so frequently made up of cells of the basal type constitutes a pitfall in histologic diagnosis, with the result that a number of such specimens have been contributed to the Registry as basal-cell carcinomas. As a matter of fact, it will be noted that there is only one carcinoma of the caruncle, that one of the squamous-cell type, in our series. As also shown in Table 4, the caruncle is a relatively common site for the nevus. It is fortunate that this portion of the eyelid is more vulnerable to benign than to malignant neoplasms, because of its physiologic importance and the difficulty of radical treatment at this site without interference with function (fig. 9).

In any series of this size there are bound to be omissions in the records. This is particularly noticeable when an attempt is made to determine the exact location of lesions of various types, and also in the evaluation of treatment; but with as large a series as this, a sufficient number of cases in each category affords adequate data from which to draw reasonably accurate conclusions.

The greatest difficulty is in obtaining the follow-up data which are so vital to the appraisal of clinical and histologic characteristics and of the effectiveness of different treatments.

Aside from the routine follow-up program conducted by the Registry Division of the Institute on all tumor cases, special effort was made to obtain information concerning the epibulbar lesions. Questionnaires were sent to the contributing physicians and hos-

TABLE 4

DISTRIBUTION OF EPIBULBAR LESIONS IN RELATION TO SITE

Diagnosis	Conjunctiva			Limbus	Cornea	Canthus		Caruncle	Other & Unspecified	Total
	Palpebral	Fornix	Bulbar			Outer	Inner			
Papilloma	14	3	58	18	5	1	8	30	1	138
Epidermidalization with and without dyskeratosis			26	32	14		1			73
Basal-cell carcinoma	5		17	3	1	3	23		1	53
Squamous-cell carcinoma	5		50	68	11	1	5	1		141
Nevus	9	1	211	60	3	2	12	33	8	339
Malignant melanoma	2	1	30	30	1	1		3		68
Dermoid, d. cyst and teratoma	2	2	43	24	8	1	2	3		82
Lymphoma	3		8					1		12
Angioma	4	1	7	1				3		16
Fibroma			7		1	1		2		11
Pterygium } Pinguecula }	1		74	37	9		4	1		126
Other lesions	15		53	9	11		7	8		100
Total	60	8	584	282	61	10	62	82	10	1159

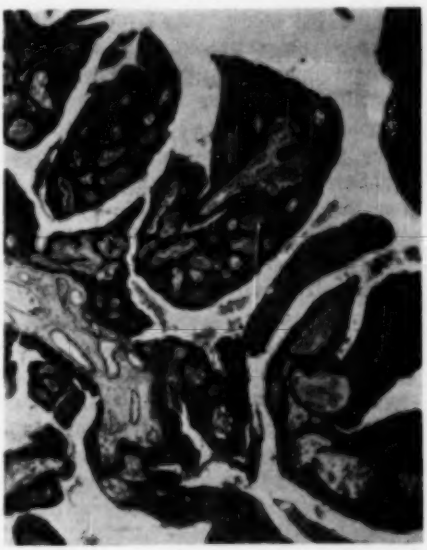

Fig. 9 (Ash). Papilloma, caruncle, basal cell type. (AIP Neg. 67112.)

pitals and to patients who had been treated while in the Army. Of the 730 questionnaires mailed, informative replies were received to 372, or 50.9 percent of them. The follow-up is particularly difficult through the specialist to whom the patient is so often referred by the general practitioner in a remote locality, and whose contact with the patient is usually lost after treatment.

Duration. As might be expected, the congenital lesions, such as dermoids and nevi, have the longest histories. In going over the individual records, however, it is surprising that a certain number of these lesions had not been noticed for periods of years. This is particularly striking in the case of open dermoids because, since they include hair shafts, they must have caused severe irritation. Seventy percent of the nevi existed for more than six months before treatment was sought. The more obvious and rapidly growing lesions, however, were predominantly of less than six months' duration.

Environmental influence. Congenital lesions and some of the incidental tumors, such as angiomas and lymphomas, naturally are not affected by the environmental factors which appear to contribute to the production of pathologic changes in the covering epithelium. These factors are heat, dryness, irritating dusts, and, perhaps of most importance, ultraviolet radiation.[3]

In the material coming from military sources during the war, the incidence of leukoplakia and carcinoma of the lip and exposed portions of the skin was high in all age groups, including the boys in their teens. Much of the training of the troops was in the southern portion of the United States, some of it deliberately in the desert areas, and a high percentage of our troops overseas were exposed to tropical conditions.

The epithelial lesions were analyzed to see if these influences could be recognized in eye material. Because of the impossibility of tracing the activities of the individual soldier from his induction to the time the specimen was removed, we had to be content with basing the geographic location on the source of the material. The inadequacy of this procedure is evident when it is remembered that soldiers who had tropical service and were invalided home because of eye lesions, might be sent to hospitals in the northern part of the country, whereupon any specimens would be contributed from the north.

Because of this confusing factor, the civilians should give a more accurate indication of the influence of environment, since their habitat is somewhat more readily established. The civilian, however, as a rule is not exposed to the detrimental environmental factors that the soldier is, except under such occupational conditions as farming.

The cases were placed in two categories: (1) Those from southern areas which include Texas, Arizona, and camps in the southern parts of the United States and the

TABLE 5

PERCENTAGE OF SOLDIERS AND CIVILIANS WITH EPITHELIAL TUMORS AND PTERYGIUM AND PINGUECULA BY GEOGRAPHIC AREA OF HOSPITALIZATION

Pathologic Diagnosis	Area of Hospitalization			
	Northern		Southern	
	Civilians	Soldiers	Civilians	Soldiers
Epithelial Epidermidalization, Carcinoma, Papilloma	82.1	76.5	76.4	67.8
Pterygium, Pinguecula	18.0	23.5	23.6	32.2

tropical areas abroad; (2) those from northern areas, both at home and abroad.

Another factor which reflects on the validity of the civilian material is that a larger proportion of cases are contributed to the Registry by southern ophthalmologists than by their northern confreres. It would seem, therefore, that the incidence among the soldiers would give a truer indication of the possible effects of environmental factors. This particular analysis was limited to the white patients, both civilian and soldier.

The data, such as they are, are condensed in Table 5. Statistically there seems to be a trend toward a slightly greater incidence of epithelial lesions in civilians than in soldiers of the northern group, and than both soldiers and civilians of the southern group; and also there appears to be a higher incidence of pterygium and pinguecula in both civilians and soldiers in the southern group, in the so-called pterygium belt.

Melanoma. The pigment tumors in this series have been grouped into malignant melanoma and nevus. In the interpretation of the histogenesis of these lesions, the theory favored has been that of Masson, who postulated that they arise from cells of the neuro-ectoderm which have melanoblastic potentialities.

Fig. 11 (Ash). Malignant melanoma at limbus. Spindle cells same type as melanoma of uveal tract. (AIP Neg. 71179.)

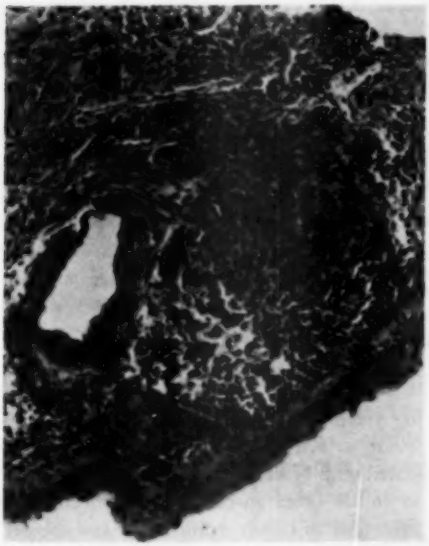

Fig. 10 (Ash). Nevus of conjunctiva showing epithelioid cells, pigmented spindle cells, and a gland inclusion. Benign. (AIP Neg. 72266.)

All of the pigment tumors are very likely congenital displacements or dysplasias of these cells. They may be manifest at birth or may lie dormant and become active in later years. Frequent mention is made in the histories of a pigmented "spot on the eye since childhood," which suddenly began to grow in adult life, and several instances in which "a small growth had been removed from the same site a number of years ago." Lesions of the group classified as nevus are more likely to be evident from birth.

A feature of conjunctival nevi which is disturbing to pathologists is the high incidence of inclusions of elements other than the simple nevus cell. These inclusions may be epithelial, most frequently in the form of glandlike elements (fig. 10), and, less fre-

TABLE 6

SUMMARY OF HISTORIES OF OCULAR TRAUMA IN PATIENTS WITH EPIBULBAR MALIGNANT MELANOMAS

AIP No.	Age at Admission	History of Trauma	Treatment	Last Known Status
22912	35	Pecked in eye by rooster in childhood.	Enucleation	Died without tumor 3 years later
26503	49	Developed in a pterygium present for years.	Enucleation	Alive, no tumor, 12 years later
40030	47	Foreign body in eye. Tumor developed 4–6 days later, increasing to 1½ cm. in diameter in 9 months.	Enucleation	In good condition 5 months later
42355	51	Struck in eye with scissors 20 years earlier. Tumor in limbus, 1 cm. in diameter, at admission. Histologically, highly malignant.	Enucleation	Alive, no tumor, 14 years later
42768	42	Eye irritated by coal dust while mining. Extensive conjunctival involvement, including orbital extension.	Exenteration	Died without recurrence or metastases, 2 years later. (Cause of death pneumonia.)
46656	59	Piece of copper in eye 20 years previously. Tumor size of pea at admission involving cornea.	Excision (subsequent recurrence with enucleation)	Died with recurrence, extension, and metastasis 4 years later
54864	45	Melanoma since childhood. Grew when eye was struck by tree at age 45. At admission, extensive conjunctival involvement and metastasis to lymph nodes.	Excision	Died with tumor, 2 months later
54945	38	Hot steel in eye at age 15, no trouble until 17 years later, when small growth on inner caruncle was noticed, but gave no trouble until 1 year prior to admission.	Excision	Alive, no tumor, 15 years later
57179	50	Particle of steel removed some years previously. At admission, history of several months rapid growth to 2 cm. diam.	Enucleation	Died, no tumor, 7 years later. (Cause of death, heart disease.)
65965	57	Hit on eyelid by stick of wood, but nodule was present on right lower lid at time. Tumor developed at limbus, apparently by extension from lid.	Exenteration	Died with recurrence and metastasis, 1 year later
67345	32	Superficial foreign body, probably metal scale. Short time afterward, tumor was noticed. Had congenital pigmentation of conjunctiva.	Enucleation	Alive without tumor, 20 months later.
70095	78	Eye scratched by thorn. Noticed small pigmented spot 2 years later, increasing in 6 months to very large growth on cornea.	Enucleation	Alive with metastasis 4 years later (1944).
78202	38	Pterygium twice operated 7 years previously. Nodule at 6 o'clock excised. Other nearby pigmented spots present. Relation to pterygium site not evident.	Excision	Alive, no tumor, 2 years later
99590	33	Struck in eye by hot cinder 5 months previously. Few days later noted 2 areas of discoloration at inner canthus, size of 2 pinheads, but enlarged rapidly.	Exenteration	No follow-up
109421	71	"Growing in a pterygium."	Enucleation	No follow-up
114085	59	Grease spattered into eye 8 years previously. Pain and growth since.	Enucleation	No follow-up

quently, hair follicles. Of the 319 nevi examined, 136 showed one or more of these inclusion elements, an observation which serves as a further indication of their congenital ectodermal origin.

The cellular composition of the malignant melanoma is practically identical with that of the uveal tumor (fig. 11), the cells varying from spindle to frankly epithelial type. There is a definite history of trauma associated with 17 of our cases of melanoma, but, as in all other instances of association of trauma with tumor, coincidence and the previous existence of a tumor must be recognized as possibilities.

A summary of the histories of trauma in

TABLE 7

SUMMARY OF DATA ON 12 PATIENTS WITH EPIBULBAR LYMPHOMAS

Accession No.	Age	Sex	Site of Tumor	Duration prior to Admission	Treatment before Admission Diagnosis	Last Known Status	Interval to* Last Known Status
028895	unknown	unk.	Bulbar conj.	Unknown	Unknown	Unknown	No follow-up
028915	66	F	Bulbar conj.	2 years	Excision and radiation	Unknown	No follow-up
055997	49	M	Bulbar conj.	Unknown	Excision†	Alive, no tumor	7 to 8 years
065157	70	F	Palpebral conj.	Up to 6 mo.	Excision, no radiation	Unknown	No follow-up
084257	45	M	Palpebral conj.	Up to 6 mo.	Excision†	Unknown	No follow-up
086394	42	M	Caruncle	Up to 6 mo.	Excision†	Alive, no tumor	6 years
087434	unknown	M	Palpebral	8 years	Excision†	Dead, no tumor	1 year
092781	35	F	Bulbar conj.	Up to 6 mo.	Excision†	Alive no, tumor	1 year
093760	45	F	Bulbar conj.	Unknown	Excision†	Unknown	No follow-up
104867	16	M	Bulbar conj.	8 years	Biopsy, x-ray & radium	Alive, tumor	3 years
109426	26	F	Bulbar conj.	Up to 6 mo.	Biopsy, local medication	Alive, tumor reduced in size	1 year
124822	6	M	Bulbar conj.	Unknown	Excision†	Alive, no tumor	4 years

* Interval from admission to last known status.
† No mention of radiation treatment.

these 17 cases is shown in Table 6. It is true that chronic irritation may be a factor in stimulating a preëxisting melanoma of the conjunctiva or a nevus of the skin to active growth, but it is just as unlikely that a single trauma can produce a tumor, especially a melanoma, in the conjunctiva as it is in any other part of the body.

Lymphoma. The pertinent data available on the 12 patients with conjunctival lymphoma are given in Table 7. It will be noted that it is a condition of advanced years, that its location is predominantly in the conjunctiva near or in the fornix, and that simple excision is adequate treatment, to judge from the limited follow-up information.

Clinically and histologically, the majority of lymphomas have been concentrations of lymphatic tissue (fig. 12), although one is of more diffuse character (fig. 13). They generally are densely packed masses of mature lymphocytes, only occasionally showing well-developed secondary follicle formation. Seldom sharply defined, they have a tendency to infiltrate the lining mucosa and, to a slighter extent, the areolar tissue.

One case had the unusual combination of lymphoma of the conjunctiva, which recurred and infiltrated rather extensively the subconjunctival areolar tissue and muscle

Fig. 12 (Ash). Lymphoma, conjunctiva, nodular type but infiltrative. Note dense packing of cells and absence of secondary follicle formation. (AIP Neg. 101665.)

(fig. 14), leading to enucleation of the eye; and malignant melanoma, which was found on examination of this enucleated eye. This patient died, but there is no account of autopsy, so that it is possible only to surmise that death was due to the metastasis of the melanoma rather than of the lymphoma.

The practical importance of such a survey as this lies in the indications to be drawn from the data as to the most effective means of treatment. Follow-up information is obviously the only guide to the success or failure of various treatments in the lesions studied and, as previously stated, this information is most difficult to collect in so large and scattered a group as this. Such information as we have to date is condensed in Table 8.

These data do not invariably correspond to those of Tables 9 through 14 for the reason that recurrences noted in interim follow-ups and successfully treated were no longer present at time of last report. The percentages of the cases in the various categories that we have been able to follow are included, so that proper appraisal may be made of the results.

The recurrence rate in papillomas is surprising. This may be accounted for by the fact that, in many of the cases, only the grossly evident papillomatous lesion was excised at operation, although epidermidalization of the conjunctival and corneal epithelium may have extended far beyond this reaction and not have been recognized by the surgeon (see figs. 2, 5, 6). The subsequent alteration of this epithelium into papilloma, dyskeratosis, or frank malignancy is possible.

The caution, therefore, may be sounded that the surgeon in his treatment of lesions of the epithelial group be guided, either before or during his surgical procedures, by a slitlamp examination of the conjunctiva to assure eradication of all the altered epi-

TABLE 8

FOLLOW-UP INFORMATION ON VARIOUS TYPES OF EPIBULBAR LESIONS*

Pathologic Diagnosis	Number of Lesions	Number of Patients Followed†	Percent Followed	Number of Recurrences	Percent Recurrences among Those Followed
Papilloma	138	33	24.	9	27.
Epidermidalization without dyskeratosis	27	9	33.	0	0.
Epidermidalization with leukoplakic dyskeratosis	27	7	22.	1	14.
Epidermidalization with Bowen's dyskeratosis	19	9	47.	3	33.
Squamous-cell carcinoma	140	70	50.	9	13.
Basal-cell carcinoma	51	14	19.	3	21.
Nevus*	359	101	24.	3*	3.
Malignant melanoma	67	47	71.	10	21.
Lymphoma	12	7	58.	0	0.
Angioma	16	6	38.	1	17.
Fibroma	11	3	18.	0	0.
Pterygium	84	19	21.	0	0.
Pinguecula	40	10	18.	0	0.
Dermoid	72	21	26.	1	5.
Teratoma	10	4	30.	1	25.
Other lesions	100	36	34.	3	8.
Total	1173	397	35.	45	11.

* This table includes recurrences reported in follow-ups but does not represent, in all cases, the last known status of the patients. For example, the one recurrence of a nevus was reported in 1943, but treatment was successful and in 1946 there had been no further recurrence.

† Includes all follow-up questionnaires to which replies were received, but some replies contained only statements as to whether patients were alive or dead, with no details as to recurrences or metastasis.

Fig. 13 (Ash). Lymphoma, conjunctiva, diffuse type. Note infiltration of epithelium and stroma and suggestions of secondary follicle formation. (AIP Neg. 101666.)

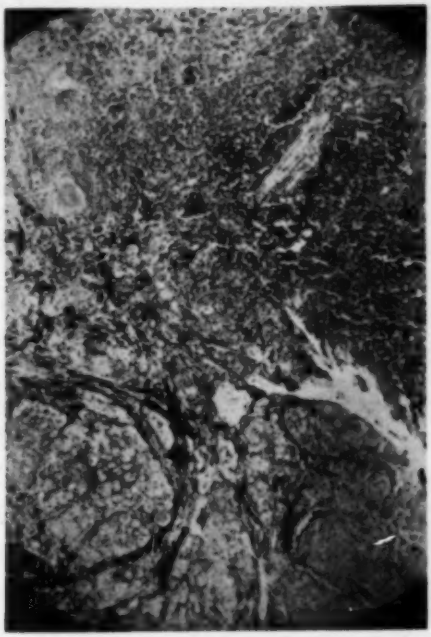

Fig. 14 (Ash). Lymphoma, conjunctiva, diffuse, infiltrative. Recurred after excision. Note infiltration of ocular muscles below and areolar tissue above. (AIP Neg. 101664.)

TABLE 9

EXCISION AND ENUCLEATION OF EPIBULBAR LESIONS AT ADMISSION IN RELATION TO LAST KNOWN STATUS OF PATIENTS*

Pathologic Diagnosis	Excision, With or Without Cautery			Enucleation, With or Without Excision		
	Recurrence and/or Metastasis	No Recurrence*	Percent without Recurrence†	Recurrence and/or Metastasis	No Recurrence*	Percent without Recurrence†
Papilloma	2	27	93.	—	1	100.
Epidermidalization	2	18	90.	—	5	100.
Basal-cell carcinoma	—	3	94.	1	1	81.
Squamous-cell carcinoma	2	29		4	21	
Nevus	1	82	99.	—	2	100.
Malignant melanoma	4	14	78.	6	17	74.
Dermoid and teratoma	—	23	100.	—	—	—
Other benign neoplasms	—	12	100.	—	—	—
Pterygium and pinguecula	—	23	100.	—	1	100.
Other lesions	3	31	91.	—	1	100.
Total	14	262	95.	11	49	83.

* This table represents only one pathologic diagnosis for each patient; in cases with more than one diagnosis the more malignant lesion was counted. Twelve patients not included in this table had cautery, exenteration, or other treatment than excision or enucleation. One of these was dead and another was dead but no details were supplied as to recurrence or metastasis; 7 were alive, with no tumor; 3 had recurrence and/or metastasis and 2 of these had died.

† Includes patients without recurrence or metastasis.

thelium. It should not be difficult to detect by this means the point at which the normal epithelium resumes. Finer alterations in vascularity can also be seen. It is the general experience that increased number or size of vessels is associated with the epithelial lesions.

In an attempt to evaluate the effectiveness of different forms of surgical treatment, Table 9 was prepared from follow-up information on 336 patients with either excision of the lesion or enucleation of the affected eye at time of hospitalization.

The significant feature of this table is the demonstration of the effectiveness of simple excision even in the malignant tumors, squamous-cell carcinoma, and malignant melanoma. Simple excision was effective in 32 of the 34 frank carcinomas and in 14 of the 18 malignant melanomas.

The percentage of recurrence and/or metastasis was slightly higher in the group of carcinomas with enucleation than those with excision, while in the two groups with malignant melanoma the recurrence rate was approximately equal. However, examination of tissues and case histories of the 22 carcinomas and the 17 malignant melanomas, in which enucleation was performed and follow-up information showed no recurrence or metastasis, indicates that simple excision should have been sufficient in at least 1 and 6 cases, respectively.

A summary of the follow-up information on 139 patients with epithelial lesions is shown in Table 10. This group includes 139 patients who have been followed from 1 to 18 years, 46 of whom had received treatment prior to admission diagnosis. Thirteen of the group, or 11 percent, of the patients on whom detailed information was available have had recurrence and/or metastasis since admission, irrespective of the extent of the lesion or the histologic evidence of malignancy. Forty-eight patients have been followed from 5 to 18 years and only three, or six percent, have had recurrence. Five of 48 had extensive lesions that were not eradicated by enucleation. One patient with squamous-cell carcinoma, upon whom exenteration had been performed, was alive with no evidence of recurrence seven years later.

Table 11 was prepared to show the last known status of 123 of the 142 patients with epithelial lesions on whom detailed information concerning recurrence or metastasis was obtained. The data are presented in relation to the surgical treatment at admission

TABLE 10

LAST KNOWN STATUS OF PATIENTS WITH EPITHELIAL EPIBULBAR LESIONS IN RELATION TO INTERVAL FROM ADMISSION TO LAST FOLLOW-UP

Status	Interval from Admission to Last Known Status							
	Number of Patients						Percent of Total	
	Less than 5 Years		5 Years or More		Total			
Alive	71		37		108		76.	
No recurrence*		59		32		91		64.
Recurrence*		5		2		7		5.
No details		7		3		10		7.
Dead	23		11		34		24.	
No recurrence*		12		7		19		14.
Recurrence*		5		1		6		4.
No details		6		3		9		6.
Total	94		48		142		100.	

* "Recurrence" refers to recurrence and/or metastasis.

TABLE 11

SURGICAL TREATMENT OF EPIBULBAR EPITHELIAL LESIONS AT ADMISSION IN RELATION TO LAST KNOWN STATUS*

Treatment for Admission Diagnosis	Last Known Status								
	Less than 5 Years			5 Years or More			Percent with Recurrence		
	Recurrence	No Recurrence	Total	Recurrence	No Recurrence	Total	Less than 5 Years	5 Years or More	Total
Excision	5	49	54	1	28	29	9.	3.	7.
Enucleation	3	18	21	1	8	9			
Excision followed by enucleation	1	1	2	—	1	1	17.	10.	15.
Other and not stated	1	3	4	1	2	3	25.	33.	29.
Total	10	71	81	3	39	42	12.	7.	11.

* Based on 123 epithelial lesions for which detailed information was obtained. Six patients were dead with recurrence, and/or metastasis, and 19 died without lesions. An additional 9 patients not shown in this table, were dead with no details as to presence or absence of lesions, and/or were living with no details given as to lesions. "Recurrence" refers to recurrence and/or metastasis.

for those followed less than five years, and those followed five years or longer. Nearly all of the recurrences and/or metastases after excision occurred within five years, indicating either that excision was incomplete or that metastasis was present at the time of hospitalization.

Table 12 summarizes the status of 49 patients with malignant melanomas in relation to interval from admission to last follow-up. Twenty-nine percent (14) of these patients had died, 14 percent without recurrence or metastasis, nine percent with tumor, and six percent with no details as to their presence or absence at the time of death. Fourteen percent of the living patients had recurrence and/or metastasis, and, in addition, nine percent had died with recurrence or metastasis; thus the total recurrence rate was 23 percent for the group on which detailed information was obtained.

The surgical treatment of the 45 patients with malignant melanomas who gave follow-up information is shown in Table 13 in relation to the latest information as to their status. Twenty-two percent of the patients

TABLE 12

LAST KNOWN STATUS OF PATIENTS WITH EPIBULBAR MALIGNANT MELANOMAS IN RELATION TO INTERVAL FROM ADMISSION TO LAST FOLLOW-UP

Status	Interval from Admission to Last Known Status							
	Number of Patients						Percent of Total	
	Less than 5 Years		5 Years or More		Total			
Alive	15		20		35		71.	
No recurrence*		11		16		27		55.
With recurrence*		3		4		7		14.
No details		1		—		1		2.
Dead	10		4		14		29.	
No recurrence*		5		2		7		14.
With recurrence*		4		—		4		9.
No details		1		2		3		6.
Total	25		24		49		100.	

* "Recurrence" refers to recurrence and/or metastasis.

TABLE 13

SURGICAL TREATMENT OF EPIBULBAR MALIGNANT MELANOMAS AT ADMISSION IN RELATION TO LAST KNOWN STATUS*

Treatment for Admission Diagnosis	Last Known Status								
	Less than 5 Years			5 Years or More			Percent with Recurrence†		
	Recurrence†	No Recurrence†	Total	Recurrence†	No Recurrence†	Total	Less than 5 Years	5 Years or More	Total
Excision	2	6	8	2	8	10	25.	20.	22.
Enucleation	3	10	13	2	3	5	23.	40.	28.
Excision followed by enucleation	—	—	—	—	5	5	—	—	—
Other and not stated	1	1	2	—	2	2	50.	—	—
Total	6	17	23	4	18	22	26.	18.	22.

* Based on 45 malignant melanomas for which detailed information was obtained. Four patients were dead with recurrence and/or metastasis, and 7 died without lesions. An additional 4 patients, not shown in this table, were dead with no details as to presence or absence of lesions, and 1 was living.
† "Recurrence" refers to recurrence and/or metastasis.

treated by excision and 28 percent of those treated by enucleation had recurrence or metastasis. Twenty-two of the 45 patients have been followed for five years or longer, and recurrence or metastasis occurred in four, or 18 percent of these.

Particularly significant is the fact that simple excision was effective in the eradication of a total of 82 of the 85 nevi and benign melanomas on which detailed information was obtained (Table 14). Only one

TABLE 14

SURGICAL TREATMENT OF NEVI AND BENIGN MELANOMAS IN RELATION TO LAST KNOWN STATUS

Surgical Treatment	Last Known Status			
	Recurrence and/or Metastasis	No Recurrence	No Details	Total
Excision	1	82	3	86
Enucleation	—	2	—	2
Cautery	—	1	—	1
Total	1	85	3	89

patient with excision had a recurrence of the lesion. Two enucleations in this group represent errors in judgment or in pathologic diagnosis. Cautery alone was used in one case, with no recurrence at last follow-up.

CONCLUSIONS

The following conclusions may be drawn from the analysis of 1,120 epibulbar tumors at the Army Institute of Pathology.

1. The basis for most of the epithelial tumors is epidermidalization of conjunctival and corneal epithelium. This altered epithelium may undergo further changes resulting in: (a) Malignant dyskeratosis, (b) papillomatosis, (c) carcinoma.

2. Epidermidalization usually extends well beyond the secondary alterations and is potential ground for recurrence if it is not removed.

3. Environmental influences, particularly drying, irritating dusts, and ultraviolet irradiation, are potent causes of epithelial and degenerative changes in the conjunctiva.

4. The inexperienced pathologist will occasionally misinterpret as malignant the benign lymphoma and the benign conjunctival nevus.

5. Conservative treatment by simple excision is effective in the majority of all epibulbar lesions that are accessible and in which damaging involvement of cornea is not included.

7th Street and Independence Avenue, S.W. (25).

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EWING'S TUMOR OF THE ORBIT*

Report of two cases

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Ewing[1] states that endothelioma of bone arises from capillary endothelium and is characterized by pseudorosettes, perithelial structure, and cords of polyhedral cells lining elongated spaces. He classifies endothelioma as: (a) Angio-endothelioma which is solitary and cystic, (b) multiple endothelioma, and (c) diffuse endothelioma or endothelial myeloma.[2] This third type is commonly described as Ewing's tumor and is characterized by its marked sensitivity to radiation.

Ewing's concept of histogenesis is by no means universally accepted, there being at least eight other theories of origin.[3] Some writers[4, 16] even doubt the existence of such a primary tumor of bone, preferring to consider the bony lesions as neuroblastoma metastases from primary lesions which frequently cannot be demonstrated. Since many subsequently proved heterogeneous conditions have at times been classified as Ewing's tumor, the diagnosis has sometimes been used as a pathologic waste basket.[16] Ewing admits that metastatic adrenal tumors present much the same structure as endothelioma of bone and states that the diagnosis of a primary endothelioma of bone can only be made in the absence of a primary soft-tissue tumor. This may require autopsy.[5, 12]

Even the characteristic response to X-ray therapy has been ascribed to metastatic neuroblastoma by some, while denied by others.[4, 6] Regardless of whether we agree with Ewing's concept of origin, we certainly have the clinical entity of a highly radiosensitive primary tumor of bone showing no osteogenesis.

Since 1939, there has been an attempt to separate a group known as primary reticulum-cell sarcoma of bone from this category.[18] The diagnosis of reticulum-cell sarcoma is based on the finding of reticulum surrounding not only lobules of cells as in Ewing's tumor but also individual cells. Response to X-ray therapy is less dramatic and the life expectancy is reported to be better than in Ewing's tumor.

This separation does not seem tenable to us. It is suggested that the greater elaboration of reticulum in the case of so-called reticulum-cell sarcoma represents simply a greater differentiation of the tumor and, therefore, a better prognosis as well as

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* Presented before the College of Physicians of Philadelphia, Section on Ophthalmology, December, 1948. The opinions and assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Navy Department.

lessened immediate sensitivity to X-ray therapy. The significance of reticulum would thus be comparable to that in malignant melanoma.[19]

Ewing's tumor comprises 10 to 15 percent of malignant tumors of bone. It characteristically occurs in early life, usually in the second decade, is more frequent in males, and is usually first noted in long bones, particularly the femur.[7, 8] The skull as a primary site has been reported infrequently (five percent).[8, 10] Neither Ewing's nor reticulum-cell sarcoma has been reported in the orbit. Early metastasis to the lungs is unusual in contrast with osteogenic sarcoma.

The earliest symptom is usually pain, intermittent in character and more severe at night. Fever and leukocytosis are often present at the onset while X-ray findings are still negative. For this reason osteomyelitis is most often suspected at this time.

Often the first symptom is a painless progressive swelling. The X-ray findings are those of an osteolytic lesion of the marrow spaces with reactive periosteal bone formation producing an "onion peel" effect. The integrity of the bone may be lost with obvious extra-periosteal infiltration in cases with negative X-ray findings, particularly in the case of flat bones. There is no typical roentgen picture of Ewing's tumor and a definite diagnosis can rarely be made from X-ray findings alone.[11]

The tumor readily breaks through the periosteum and freely invades adjacent tissues. Pain is probably present only while the tumor is confined by and is stretching the periosteum. At biopsy, a highly vascular dark-red or grayish tissue of variable consistency is found which may grossly resemble granulation tissue. Necrosis is often found histologically and may account for the frequently observed variation in the size of the tumor during its course.

In the differential diagnosis, osteomyelitis or periostitis is most likely to be suspected if the case is seen early. After the disease has lasted some time, other primary tumors of bone, neuroblastoma, and bony metastatic lesions must be considered.[15, 17]

In order to establish the diagnosis clinically the following criteria must be met:

1. Exclude a primary soft-tissue malignancy by thorough examination of the entire body.

2. Obtain a biopsy with characteristic histopathologic findings.

3. Presence of osteolytic lesions showing exceptional sensitivity to radiation therapy.

The prognosis in Ewing's tumor is poor. Average life expectancy is 1 to 3 years but the diagnosis is seldom made until a year after onset of symptoms.[13] In rapidly fatal cases, death may occur within six months from onset of symptoms. With radiation therapy, 10 percent of the patients attain a cure of up to five years, and the American College of Surgeons Registry of Bone Sarcomas records one case with a 31-year survival.[2, 14] Amputation with radiation to the regional lymph nodes is still recommended by some authors.[18]

Case reports

Case 1

History. J. P. D., a 24-year-old white man, was admitted to an Army General Hospital on July 23, 1945, with a four months' history of pain in the right groin, limping, and a 10-pound loss in weight. X-ray examination revealed an extensive destructive process involving the right acetabulum and innominate bone. The X-ray impression was that of a malignant bone tumor, probably osteogenic sarcoma. The possibility of Ewing's tumor was also mentioned.

There were no significant laboratory findings. A biopsy was taken from the right iliac region and the pathologic diagnosis of reticulum-cell sarcoma was made and confirmed by the Army Institute of Pathology.

The patient was started on radiation therapy on August 7, 1945, and received a total of 3,600 r to the right pelvic region over a period of 21 days.

Four months later, after being discharged

from the Army, he noticed a small mass over the lower right jaw which became progressively larger followed shortly by proptosis of the right eye. A dull ache was first noted seven weeks after onset of swelling and five days before admission to U. S. Naval Hospital, Philadelphia, on January 31, 1946.

Admission examination revealed a hard nontender diffuse swelling of the right mandible. There was a moderate soft-tissue swelling of the lateral orbital wall overlying the orbital process of the zygoma. The right eye was displaced forward 7 to 8 mm., downward 3 to 4 mm., and medially, 3.0 mm. The conjunctiva of the lower inner angle was pushed forward over the lid margin, covering the lower punctum and causing marked lacrimation (fig. 1).

Ocular rotations were limited in all directions so that single binocular vision was present only within a 15-degree range. Vision was 20/20, O.U. Examination of the globe itself was essentially negative.

X-ray examination on February 2, 1946, revealed a destructive process, moth-eaten in appearance, involving the body and ramus of the right mandible (fig. 2). The right zygomatic bone showed a similar but less evident moth-eaten appearance. Pelvic roentgenograms revealed an extensive destructive process involving the right acetabulum and the greater part of the innominate bone. There was no evidence of lung or bony involvement elsewhere in the body.

Impression: "Ewing's tumor and reticulum-cell sarcoma must be considered."

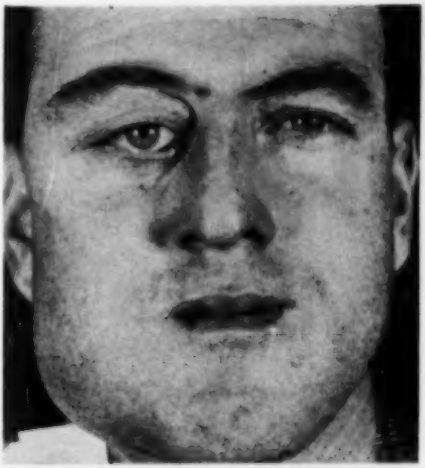

Fig. 1 (Harbert and Tabor). *Case 1.* Appearance of patient on admission.

Laboratory findings. Urinalysis revealed no Bence-Jones protein. A biopsy was taken from the tumor mass at the angle of the right mandible. The tissue was grayish red,

Fig. 2 (Harbert and Tabor). *Case 1.* X-ray film revealed the moth-eaten appearance of the destructive process which involved the body and ramus of the right mandible.

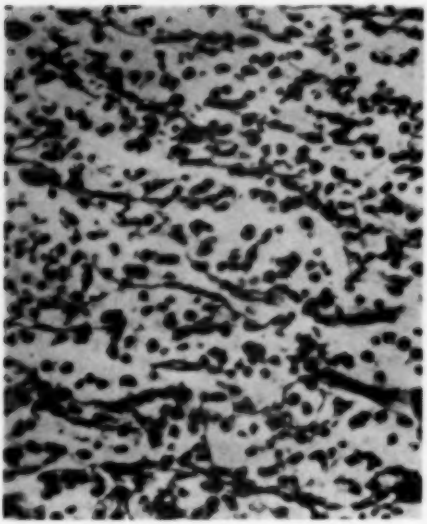

Fig. 3 (Harbert and Tabor). *Case 1.* Reticulum stain, showing well-marked elaboration of reticulum.

vascular, and friable. Microscopic section showed tumor cells ranging from small ovoid dark-staining cells with scanty cytoplasm to larger oval-shaped cells, showing a moderate number of mitotic figures. The cells were supported upon a fairly abundant reticular connective tissue which contained a relatively sparse blood supply. Reticulum stains showed that large lobules of tumor cells were surrounded by reticulum rather than individual cells.

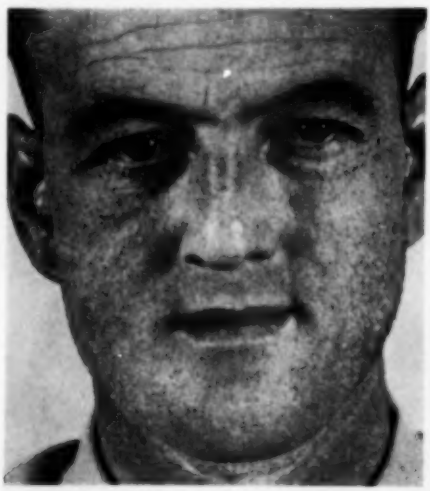

Fig. 4 (Harbert and Tabor). *Case 1.* Appearance of patient after radiation therapy.

Pathologic diagnosis. Endothelial myeloma (Ewing's tumor) (fig. 3).

Radiation therapy was commenced on February 9, 1946, and the patient received a total of 2,400 r to the right jaw and orbit over a 20-day period. There was immediate and dramatic response to therapy, although complete recession did not occur until treatment was finished (fig. 4). He was discharged as an in-patient on March 1, 1946. Between March 3, 1946, and April 2, 1946, a period of 29 days, he received an additional 3,000 r to the right innominate bone as an out-patient.

Since discharge, this man has been in excellent health, and there has been no evidence of recurrence to date.

Recent follow-up examination reveals the vision to be 20/20, bilaterally; there is full ocular motility and no proptosis. Fundi and fields are normal. There has been no weight loss. X-ray examination shows complete disappearance of the neoplastic disease from the right zygomatic bone, the body of the right mandible, and right innominate bone. The only evidence of previous disease is coarsened trabeculations.

Case 2

History. J. L. W., a young white man, aged 19 years, was first admitted to a naval hospital on May 21, 1946, because of proptosis of the right eye and a smooth circumscribed swelling in the right temporal fossa. X-ray examination of the orbital region was negative at that time. A biopsy was taken from the temporal tumor and the pathologist's report was "inflammatory granulomatous tissue with marked endothelial proliferation." He was transferred to the U. S. Naval Hospital, Philadelphia, on August 3, 1946.

Examination at that time revealed a

marked proptosis of the right eye without apparent lateral or vertical displacement. The palpebral fissure could not be closed. There was diplopia in all fields of gaze. There was a smooth circumscribed swelling of the right temporal fossa showing the scar of the previous biopsy (fig. 5). The remainder of the ophthalmic examination was not remarkable. Vision was: O.D., 20/50, O.S., 20/20. Visual fields were normal.

X-ray examination of the right orbit showed no obvious osteolytic defect. Roentgen survey of the entire body revealed no evidence elsewhere of a primary tumor or metastases.

Fig. 5 (Harbert and Tabor). *Case 2.* Appearance of patient on admission.

On August 10, 1946, a biopsy was taken from the temporal tumor mass. The tissue was dark red, highly vascular, soft, and friable. No bony defect was palpable. Microscopic section showed localized groups of cells of uniform size and shape with many new blood vessels. The cells were somewhat polyhedral with light-staining nuclei and pale cytoplasm. The cells were arranged in cordlike masses surrounding elongated spaces. Review of slides from the original biopsy showed similar structure.

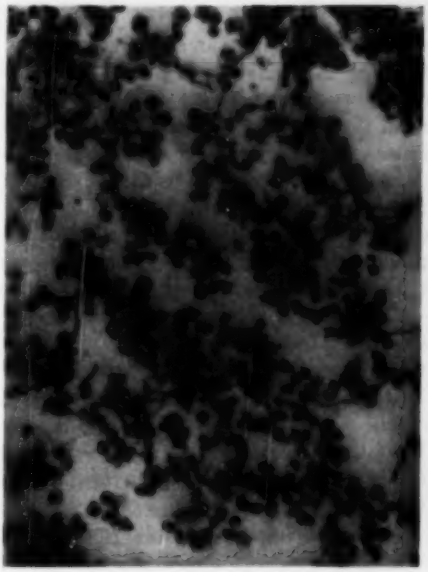

Fig. 6 (Harbert and Tabor). *Case 2.* Reticulum stain, showing paucity of reticulum.

Pathologic diagnosis. Ewing's tumor (fig. 6).

Radiation therapy. Between August 16 and 30, 1946, a period of 14 days, the patient received a total of 3,000 r to the right temporal area. Within a week the tumor had

Fig. 7 (Harbert and Tabor). *Case 2.* Appearance of patient after radiation therapy.

practically regressed (fig. 7). There was restoration of binocular single vision in all fields of gaze and the vision of the right eye returned to normal. He was discharged from the Navy on December 28, 1946, because of the poor prognosis.

Follow-up reports on this man reveal that four months later he was admitted to a veterans hospital because of recurrence of the proptosis on the right. He pursued a downhill course during the following six months.

The right eye was enucleated and a biopsy was taken from the retrobulbar mass. This was followed by X-ray therapy consisting of 3,000 r with regression of the mass. Report of the biopsy was reticulum-cell sarcoma. He died on October 16, 1947 with clinical evidence of metastases to many regions of the body.

Final pathologic report following autopsy was retrobulbar sarcoma, right, with extension to orbit, skull, and brain, and metastases to lungs, liver, ribs, sternum, vertebras, and bony pelvis.

Comment

Microscopic slides, including reticulum stains of biopsy specimens from the first case and autopsy material from the second, were carefully reviewed by Commander T. B. Bennet (MC) U.S.N., and Dr. Clark E. Brown, Dr. Robert F. Norris, and Dr. R. Philip Custer. The consensus was that the pathologic findings in both cases were consistent with the diagnosis of Ewing's tumor. It is interesting to note that the paucity of reticulum in the second case corresponded with the poor outcome, while the first case with the greater elaboration of reticulum is having a more benign course.

Summary

1. Two cases of Ewing's tumor involving the orbit are reported, apparently for the first time. The term, Ewing's tumor, is used to describe the clinical entity of a highly radiosensitive primary tumor of bone showing no true osteogenesis.

2. One of these cases was primary in the orbit with a rapidly fatal termination in spite of dramatic immediate improvement with radiation therapy. The other case was secondary in the orbit with complete replacement of osteolytic defects by normal cancellous bone following X-ray therapy and freedom from recurrences to date, a period of three years and five months.

3. Prognosis of Ewing's tumor is considered inversely proportional to the degree of elaboration of reticulum.

4. Ewing's tumor and reticulum-cell sarcoma are considered to be identical in histogenesis.

U. S. Naval Hospital (45).

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STREPTOTHRIX AS A CAUSE OF FOLLICULAR CONJUNCTIVITIS AND OTHER OBSCURE CONJUNCTIVITIDES*

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Obvious infection of the canaliculus with the higher bacteria known as streptothrix is not uncommonly encountered in ophthalmic practice. Its classical clinical picture would not appear to warrant any special comment. However, it is generally not realized that a subclinical canaliculitis due to this organism may result in various types of obscure and obstinate conjunctivitis, in instances in which the tear passages appear entirely normal. Usually these cases resemble those due to ordinary chronic bacterial conjunctivitis. Sometimes, though, the appearance is somewhat different. There are a few reports in the literature in which follicular conjunctivitis occurred; each case was considered to be and treated as trachoma for a long period of time.

It is the purpose of this paper to report another such rare case of follicular conjunctivitis due to streptothrix and also to point out some simple office laboratory procedures that are valuable in the early diagnosis of less obvious cases of this not too rare type of infection.

REPORT OF A CASE

History. A woman, aged 48 years, was referred for special studies because of a follicular conjunctivitis, in the right eye only, of at least three months' duration. In the course of previous treatment her tear passages had been exonerated because of the fact that on two occasions they had irrigated freely. Routine cultures had revealed toxic staphylococci yet intensive antistaphylococcal therapy had not helped. Epithelial scrapings had not been made.

On examination of the right eye no obvious discharge was noted. The lacrimal puncta and canaliculi appeared perfectly normal. The conjunctiva of both the upper and lower lids and of the fornices had a granular appearance due to the presence of numerous grayish-white follicles. No preauricular lymphadenopathy was noted. The eye was otherwise normal.

The left eye showed no abnormalities.

Cultures of the conjunctiva revealed, as previously, a few colonies of toxic staphylococci. Epithelial scrapings, stained by the Giemsa method, revealed numerous polymorphonuclear leukocytes containing minute coccoid particles resembling staphylococci, but smaller in size. In addition, extracellular filamentary forms and micrococci, often in chains, resembling small streptococci, were found (fig. 8).

These findings strongly suggested the presence of higher bacteria. Because of this, despite their normal appearance, after the upper and lower lacrimal puncta were dilated, the canaliculi were expressed and purulent discharge was obtained which showed

* Read before the New York Society for Clinical Ophthalmology, February, 1948. From The Mount Sinai Hospital and the Manhattan Eye, Ear, and Throat Hospital.

streptothrix on smear (fig. 6). Determined curetting then was productive of a small concretion in both the upper and lower canaliculi. Once these were removed and one-percent iodine was injected into the canaliculi, the conjunctival inflammation began to improve immediately and the follicles disappeared entirely within three weeks.

Discussion of case

Follicular conjunctivitis due to streptothrix infection has, in practically every reported instance, been treated unsuccessfully as trachoma for long periods of time, often many years. The reported cases may be divided into two groups. In the first type, a typical streptothrix canaliculitis is ultimately discovered. In the other category, the infection is limited to the conjunctiva and no involvement of the lacrimal apparatus occurs. Morax,[1] Rutberg,[2] Kalaschnikow,[3] and Valière-Vialeix,[4] all have reported cases in many ways similar to mine, that is, of the first kind. An instance of long-standing papillary conjunctivitis, considered trachomatous, which finally turned out to be due to streptothrix canaliculitis was reported by Sabata.[5]

However, only in the case of Morax was the clue provided by the laboratory findings belatedly appreciated. In the other cases it took up to 12 years for canalicular swelling to become clinically apparent and to point to the etiology.

In the second group of cases reported, those in which the tear passages are not involved and the follicular conjunctivitis is due solely to conjunctival infection, as in the cases of Knapp and Dwyer,[6] and of Liegard,[7] the clinical course differed from the other type in that pre-auricular adenopathy was prominent, and the condition was fundamentally acute. Furthermore, instead of the typical streptothrix, nocardia was cultured by Liegard.

It seems to me that these cases, as well as several other allied nonfollicular cases (Liegard and Landrieu[8] and May[9]), really were instances of Parinaud's oculoglandular syndrome due to other types of higher bacteria —not "streptothrix foersteri." This second group should not be included as examples of what we consider follicular conjunctivitis due to streptothrix.

The follicular response

The follicular response in the case reported, and in the others like it, may be explained as a lymphoid reaction to the toxins presumably produced by the streptothrix. Thus under Morax's classification[10] it would be considered a toxic follicular conjunctivitis. Although not the usual type of reaction, follicular hypertrophy can occur even in bacterial conjunctivitis, especially in individuals who have a lymphoid diathesis (Thygeson[11]). I, myself, have seen it occur in acute staphylococcal conjunctivitis.

The organism

The name "streptothrix foersteri" was given by Cohn, in 1875, to the higher bacteria he had discovered in the lacrimal canaliculus, despite the fact that Corda, in 1839, had used the term "streptothrix" to denote an entirely different group of fungi.[12] Actually, the organism found in the canaliculus is an actinomyces of low virulence. Thus it would appear, at first glance, inadvisable to continue to call this organism "streptothrix." However, since the benign, unique picture it produces in the canaliculus is so different from that of infections with other strains of actinomyces, we feel that the term streptothrix foersteri should be used to designate an organism causing a very special type of disease.

It has been thought that the infection is airborne with the organisms lodging in those canaliculi which contain diverticula.[13] Thygeson[14] points out the large number of canaliculi that have such diverticula. Emmons[15] has recently shown, however, that actinomyces bovis exists as a saprophyte in the crypts of tonsils and on discharge from these it may be spread to other susceptible tissues. The possibility of spread from the

mouth to the eye has been postulated long ago.[16]

Clinical forms

From a clinical point of view it is advantageous to classify streptothrix infections of the conjunctiva as follows:

Group 1. Bulbar type

In certain parts of the world, especially in Egypt, the infection is manifested by the occurrence of nodules on the bulbar conjunctiva. These nodules are filled with streptothrix and disappear even if only partly ex-

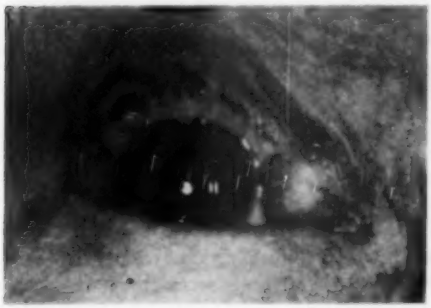

Fig. 1 (Theodore). Streptothrix infection of long standing, involving the upper canaliculus. (Case of A. R.)

cised.[17] The canaliculi are not involved. This type apparently does not occur in the United States.

Group 2. Palpebral conjunctivitis with obvious involvement of the canaliculus

This type should hardly be confused with any other condition yet its manifestations are often mistaken for styes, chalazia, infected sebaceous cysts, or nonmycotic infections of the canaliculus. As is well known, streptothrix canaliculitis occurs predominantly in women, and involves the upper canaliculus, either independently or in conjunction with the lower, in at least one third of all cases.

Fig. 2 (Theodore). Streptothrix infection involving the lower canaliculus. (Case of W. K.)

Thus it may be stated that:

A. Unilateral swelling in the region of the inner canthus, especially in the upper lid in women, should immediately arouse suspicion and focus attention on the puncta, which are generally patulous or slightly dilated in this condition (figs. 1 and 2).

B. If, on milking of the canaliculus, some fluid or purulent discharge is noted, the diagnosis is 99 percent certain (fig. 3).

C. If, on further expression, a concretion is obtained, the diagnosis, from a clinical point of view, is absolutely certain (fig. 4). In this group laboratory examination is generally not necessary for diagnosis.

Sometimes ordinary bacterial skin infec-

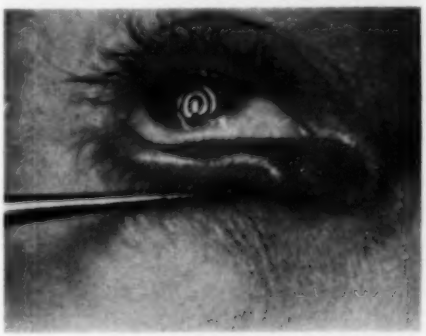

Fig. 3 (Theodore). Same case as shown in Figure 2. Pus is exuding from the lacrimal punctum, after dilation and expression. (Case of W. K.)

Fig. 4 (Theodore). Same case as shown in Figures 2 and 3. Fragments of broken streptothrix concretions are visible above the punctum, near the inner canthus and, just below the applicator, on the skin. (Case of W. K.)

tion about the canaliculi may simulate the picture, but here nothing is expressed. One case was encountered in which a rare true canaliculitis due to the staphylococcus was present. Here a little pus was expressed, but no concretions. The bacteriology and subsequent course confirmed the clinical impression of nonmycotic infection.

It should also be mentioned that obstruction of the lacrimal passages does not have to, and often does not, occur in this group.

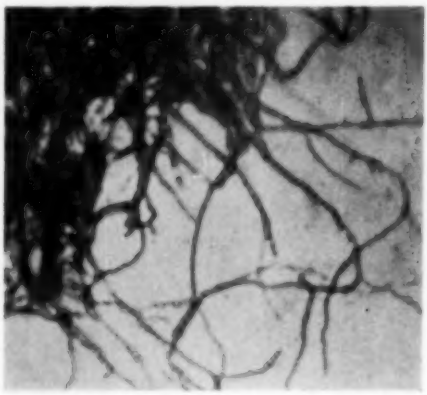

Fig. 5 (Theodore). *Streptothrix*. Photomicrograph of a stained crushed streptothrix concretion, showing branched mycelia and beading. (Case of J. A.)

Group 3. Cases in which only conjunctival signs are present and the canaliculi appear normal

As mentioned earlier in this paper, these cases are generally not properly diagnosed until obvious canalicular swelling occurs, which sometimes takes years. The early picture may simulate any common type of conjunctivitis. If simple laboratory tests are performed, however, the diagnosis can be made readily.

Office laboratory aids in the diagnosis

For practical purposes cultures are not particularly helpful nor generally necessary. Anaerobic methods, as well as procedures to eliminate bacteria such as staphylococci, are required to get positive results. Furthermore, even when successful, growth is slow and takes weeks to appear.

Secretion smears and epithelial scrapings, on the other hand, are of the greatest value, and can easily be performed in any office equipped with a microscope. The streptothrix, like other actinomyces, grows in branched mycelia which fragment into coccoid, bacillary, and filamentous forms. All forms are Gram positive and stain readily with the usual bacterial stains as well as the Giemsa stain used routinely for epithelial scrapings.

The findings, therefore, are:

1. *On crushing a concretion.* The branched mycelium has a "Medusa-Head" (fig. 5).

2. *Secretion smears.* Purulent exudate containing (a) long, thin, beaded bacilli, often in chains; (b) long, fine filaments; (c) numerous dots (coccoid form), resembling micrococci, but smaller, often looking like chains of minute streptococci. All the elements described show uneven, often polar, staining (figs. 6 and 7).

3. *Epithelial scrapings.* A purulent exudate, with coccoid elements found predominantly intracellularly, while filaments and bacilli are scattered about extracellularly (fig. 8).

Treatment

The essential procedure in the cure of streptothrix canaliculitis is the removal of all the concretions, followed by copious lacrimal irrigations. Treatment is thus mechanical rather than chemical. In order to get out all the concretions, expression alone is

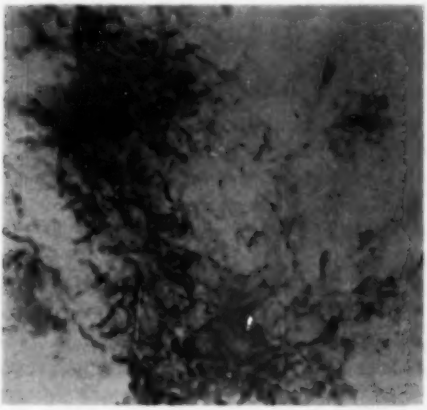

Fig. 6 (Theodore). *Streptothrix.* Photomicrograph of pus from the canaliculus showing mainly filamentous and bacillary forms, with polar staining. (Case of R. S.)

generally not enough. It is better to dilate the punctum and curet the lining of the canaliculus. To do this properly, infiltration of procaine into the adjacent tissues and slitting of the punctum sufficiently to allow the insertion of a small currette is advised.

After all the concretions are removed, a few drops of one-percent tincture of iodine may be instilled into the canaliculus by means of a lacrimal syringe and cannula.

Aqueous penicillin, five-percent sodium proprionate solution (Theodore[18]), one-percent sodium iodide or a sulfonamide, all of which appear to be effective against actinomyces, may then be prescribed for home use.

These medicaments will not be completely efficacious if all the concretions have not been removed; they will only ameliorate the condition. Actually, if the concretions have

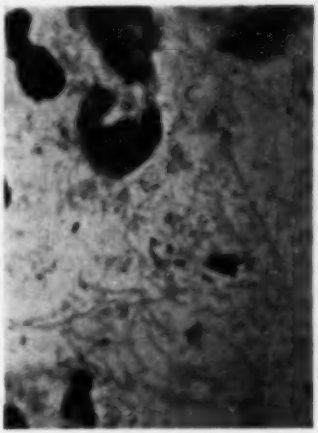

Fig. 7 (Theodore). *Streptothrix.* Photomicrograph of conjunctival smear, showing mainly branched bacillary forms. (Case of J. A.)

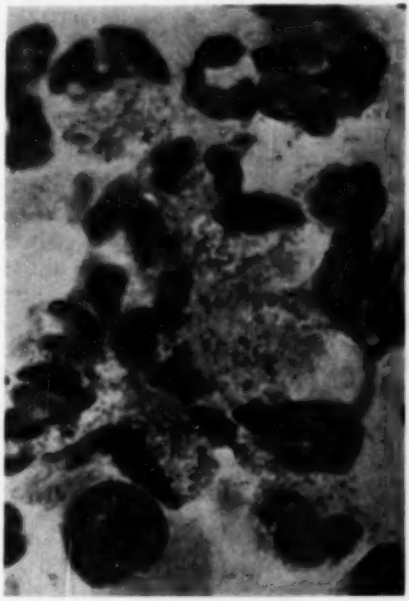

Fig. 8 (Theodore). *Streptothrix.* Photomicrograph (Giemsa stain) of epithelial scraping of upper lid, showing pus cells which contain coccoid-fragmented forms. (Case of R. G.)

been properly taken care of, a placebo such as boric-acid solution will do, although antibiotics are naturally preferable on theoretic grounds, in order to eliminate the few bacteria remaining in the canaliculus. A few thorough lacrimal irrigations of at least 10 cc. of saline or sodium propionate performed with the head bent down, chin against the neck,[19] should then be done at intervals of 2 to 3 days to insure against recurrences.

Summary

Streptothrix infections of the canaliculus are not uncommonly encountered in ophthalmic practice. Cases in which obvious involvement of the canaliculus occurs should be readily diagnosed on clinical grounds alone. It should be stressed however, that subclinical involvement of the canaliculi may give rise to obstinate, obscure types of conjunctivitis that may last for years unless the cause is discovered. A case of follicular conjunctivitis due to streptothrix is reported and office laboratory aids in the recognition of this higher organism are described and shown by photomicrographs.

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THE EFFECT OF ACTH IN GLAUCOMA*

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INTRODUCTION

There is a rapidly growing literature concerning the effect of the adrenocorticotropic hormone, ACTH, in various ophthalmic diseases, but so far as is known no study of the response in primary glaucoma has been made. Therefore, with no preconceived ideas as to its efficacy in this disease, a pilot experiment was undertaken, feeling that even a negative result would be of value. Whether or not, in primary glaucoma, the ocular hypertension would react to such a stimulus as the alarm or stress reaction, such as that elicited by the injection of ACTH, seemed doubtful. Since there is some evidence, however, that a disturbance of the hypothalamus occurs in glaucoma we were encouraged to try this experiment.

Our first two cases of primary glaucoma showed that the hormone had no appreciable effect upon the intraocular pressure.

The third patient presented the unusual conditions of uveitis in one eye developing in what was considered to be primary bilateral glaucoma. Here the acutely raised tension and inflammation responded promptly in the one eye.

In order to confirm observations made by others, we accepted for our fourth patient a case of early uveitis with a secondary rise in tension and observed a remarkable clinical improvement within 48 hours, including a definite drop in tension.

The fifth case was one of chronic primary glaucoma, which, after eight days of treatment, showed no significant drop in pressure.

* From the Section of Ophthalmology, Department of Surgery, School of Medicine, Yale University. Funds for this experiment were contributed by the National Society for Prevention of Blindness, National Committee to Combat Blindness, and Gift-National to Combat Blindness.

TECHNIQUE

The patients were placed on a salt-free diet 24 hours before admission and continued on this diet for the duration of the hospital treatment. All miotics were withheld during this study. Routine laboratory studies and eosinophile counts were made. Electrolyte studies were made by the Department of Internal Medicine. Daily intake and output, weight, and blood pressure were recorded. Intraocular pressures were taken every four hours for the entire period with the standard Schiøtz tonometer. Fields were taken before, during, and after the treatment. At the end of the first 24 hours of hospitalization 20 mg. of ACTH were administered every six hours. The total doses of ACTH ranged from 240 mg. to 620 mg.

CASE REPORTS

CASE 1

E. P. was a 53-year-old Negress, first examined in 1941 because of blurred vision and headaches. Vision was 17/20, O.U., uncorrected. The tension was: O.D., 30 mm. Hg (Schiøtz); O.S., 28 mm. Hg. Deep cupping of both discs was noted. The patient was started on pilocarpine hydrochloride (0.5 percent, three times daily) and gradually increased to four percent because of a rapid decrease in visual fields.

On admission to the hospital, miotics had been withdrawn for two days at which time the tension was: O.D., 32 mm. Hg (7.5/4.5); O.S., 26 mm. Hg (7.5/6) (Schiøtz). Vision, corrected, was: O.D., 20/15—2, O.S., 20/20. Gonioscopy showed narrow angles, bilaterally. The impression was that of a primary low-tension glaucoma.

The patient was placed on ACTH, 20 mg. every six hours, with no significant drop in tension, so that on the third hospital day the

patient was given an additional 20 mg. A total of 360 mg. was given with no appreciable effect on the intraocular pressure.

CASE 2

J. R. was a white man, aged 59 years,

Fig. 1 (Blake, Fasanella, and Wong). *Case 1.* E. P., a Negress aged 53 years, had primary low-tension glaucoma. A total of 360 mg. ACTH failed to produce any therapeutic response in the right eye.

whose left eye had been enucleated because of injury. Primary glaucoma was diagnosed in the right eye in October, 1949, and treatment with pilocarpine was commenced. Tension on November 15, 1949, was 35 mm. Hg (5.5/2) (Schiøtz). Field study showed peripheral contraction, enlarged blindspot, Bjerrum scotoma, and Roenne step. Pilocarpine (3.0 percent) was ordered every three hours. Vision was 5/200 (corrected) due to myopia and lens changes.

Gonioscopic examination showed a narrow angle, no synechias, no iris atrophy. The fundus was not seen.

Since no definite drop in intraocular pressure was observed after four days, it was concluded that the hormone had no effect upon this case of primary glaucoma. A total of 240 mg. of ACTH was administered.

CASE 3

L. S., a 55-year-old white man, was seen on April 15, 1950, because of pain and blurred vision of the left eye.

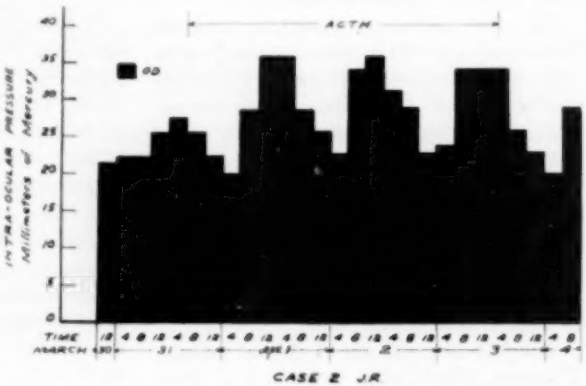

Fig. 2 (Blake, Fasanella, and Wong). *Case 2.* J. R., a white man, aged 59 years, had primary glaucoma. A total of 240 mg. of ACTH was administered with no decrease in the intraocular pressure.

Past history. During July, 1949, the patient developed an acute uveitis of the left eye, with secondary hypertension up to 55 mm. Hg (Schiøtz), and was treated by a

competent ophthalmologist. Careful studies failed to reveal any etiologic agent. Paracentesis was required three times to reduce the tension. The tension finally became normal with vision of 20/20. The right eye showed no increased tension or evidence of uveal disease at that time.

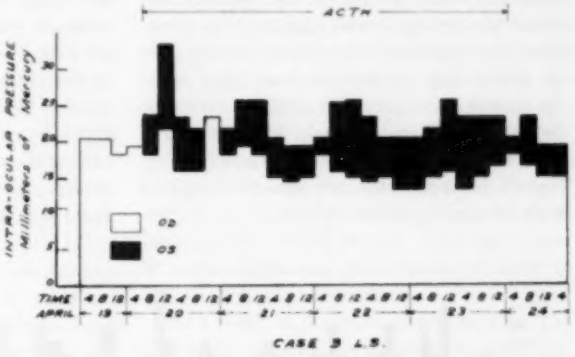

Fig. 3 (Blake, Fasanella, and Wong). *Case 3.* L. S., aged 55 years, was a white man with a history of bilateral primary glaucoma and subsequent uveitis of the left eye. The intraocular pressure, O.S., was brought to normal levels within 24 hours with ACTH. A total of 350 mg. was administered.

Present illness. On April 15, 1950, the patient appeared at the Emergency Room of the New Haven Hospital because of pain and marked diminution of vision of the left eye of one day's duration.

Biomicroscopy was negative in the right eye, but the left eye showed a steamy cornea, large pigmented keratic precipitates, an irregular pupil, posterior synechias, and atrophy of the iris in the 7- to the 9-o'clock position.

Vision on admission was: O.D., 20/25; O.S., hand movements. Tension was: O.D., 40 mm. Hg (Schiøtz); O.S., 56 mm. Hg. A paracentesis of the left eye was performed.

On April 19th, the tension was: O.D., 30 mm. Hg; O.S., 37 mm. Hg. The patient was admitted to the hospital for study and treatment with ACTH. A total of 350 mg. was administered.

Upon discharge, April 24th, vision was: O.D., 20/15; O.S., 20/30. At that time tension was: O.D., 22 mm. Hg; O.S., 27 mm. Hg.

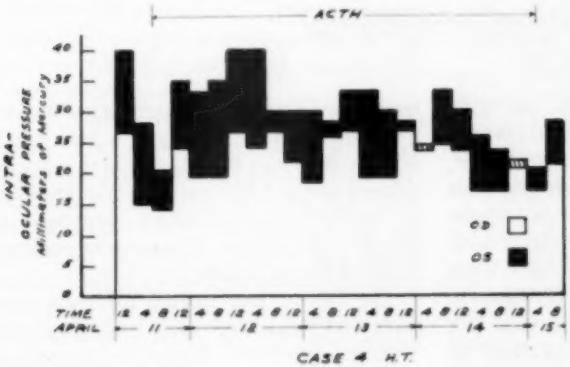

Fig. 4 (Blake, Fasanella, and Wong). *Case 4.* H. T., a white man, aged 53 years, had uveitis of the left eye. The intraocular pressure under ACTH therapy dropped to normal levels within 60 hours. A total of 280 mg. was administered.

CASE 4

H. B. T., a white man, aged 53 years, had had chorioretinitis in the left eye in 1914 with recurrences in 1927 and 1937. Thorough

study revealed no cause unless the presence of Streptococcus viridans found in prostatic secretion after massage could so be considered.

Present illness. Because of slight urinary frequency early in April, the patient consulted his urologist who massaged the prostate. No organisms were found at that time on smear and culture but, two days later, the patient presented with an acute uveitis of the left eye. Keratic precipitates, cells, and flare were present and tension was 30 mm. Hg (Schiøtz) in the left eye as compared with 19 mm. Hg in the right eye.

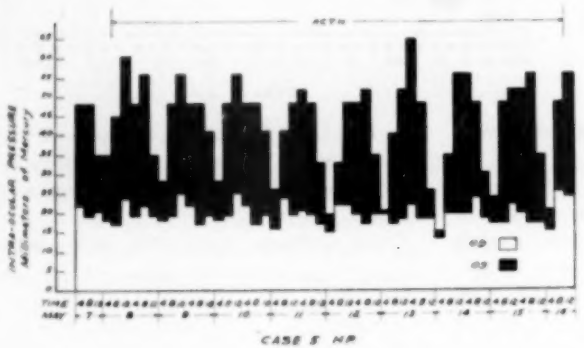

Fig. 5 (Blake, Fasanella, and Wong). *Case 5.* H. P., a white woman, aged 49 years, had chronic, simple glaucoma, O.U. Therapy with ACTH for eight days, comprising a total of 620 mg., failed to lower the intraocular pressure.

The patient was admitted to the New Haven Hospital on April 10, 1950. Within 48 hours after administration of ACTH, the marked congestion of the left globe had practically disappeared, keratic precipitates had decreased, and the pupil dilated well. Tension, which dropped to normal levels within 60 hours, was as shown in Figure 4.

Three weeks later the uveitis was still clearing and tension was 19 mm. Hg. The total amount of ACTH administered was 280 mg.

Case 5

H. P., a 49-year-old white housewife, was admitted to the ward service with the diagnosis of chronic simple glaucoma, O.U. The patient had been extremely uncoöperative in not using her medication, in failing to report for fields, and in refusing surgery.

Present illness. She was first seen in the Eye Clinic in December, 1940, at which time her uncorrected vision was: O.D., 17/20; O.S., 17/200. In July, 1947, her vision without glasses was: O.D., 20/50; O.S., 20/100. The patient complained of blurring in the left eye of two months' duration. The tension at that time was: O.D., 19 mm. Hg; O.S., 30 mm. Hg (Schiøtz).

On March 30, 1950, the patient was seen in Special Glaucoma Clinic and the vision recorded was: O.D., 20/20; O.S., hand movements. Gonioscopic examination showed a narrow angle in both eyes. A field in the left eye showed a Roenne step with a 2-mm. white target at 1,000 mm. The field was done in the right eye. A field was impossible to obtain in the left eye. There was no evidence of uveal disease in either eye.

The patient was treated for eight days with ACTH, and received a total of 620 mg. without significant change in intraocular pressure.

Additional cases

Since Cases 1 to 5 were reported, three additional cases have been treated.

The first was that of a 57-year-old woman who had had a chronic uveitis of the left eye, and whose ophthalmologist urged a trial

test with ACTH. The intraocular pressure was 44 mm. Hg (Schiøtz) upon admission. During the five days of ACTH administration (80 mg. daily) the tension dropped to an average of 24 mm. Hg. Within four days of termination of treatment, the pressure rose to 60 mm. Hg, indicating that the hormone had cleared the uveal tissue to a certain extent but could not eliminate the organized structural changes of the earlier attack.

The second patient was a healthy man aged 38 years, who had had primary bilateral glaucoma of six years' duration. A sclero-iridectomy had been performed on each eye, with normalization of tension in the right eye but not in the left. He was administered 280 mg. of ACTH during the four days of treatment without appreciable lowering of tension and was readmitted for further surgery.

The third case is of particular interest. Three years ago, a woman, now aged 58 years, had had bilateral iridectomies for glaucoma, followed by cataract formation and extraction of both lenses. When seen by one of us (E.M.B.) in December, 1948, vision was nil in the left eye and 22/100 in the right. Sympathetic uveitis was diagnosed, the left eye was enucleated, and vision rose to 20/20 with normal tension.

Her condition remained unchanged until June, 1950, when a sharp acute attack of glaucoma developed. The intraocular pressure was 75 mm. Hg (Schiøtz) upon admission to the hospital. ACTH (80 mg.) was administered daily with a slight lowering of pressure for four days. A more marked fall followed, and by the sixth day tension dropped to 20 mm. Hg where it has remained to date.

Discussion

The doses administered appeared adequate as evidenced by the prompt and sustained decrease of circulating eosinophiles. In several of the cases, the dosage of the hormone was increased on one day to 100 mg. with no evidence of untoward reaction at any time or in any case. The duration of treatment varied from 4 to 8 days, being limited by the supply of ACTH. The absence of any marked changes in the intraocular pressure in the cases of primary glaucoma in contrast to the sharp response in the cases of uveitis with hypertension would suggest that the duration of treatment was adequate in the former group.

An unexpected finding in all these cases under treatment was the unusual diurnal variation in ocular tension with observed high points during the day and low points at night. This was particularly striking in the primary glaucoma cases.

As a result of the administration of ACTH is Case 3, it would seem that the condition which had appeared to be primary glaucoma of the right eye was probably a low-grade involvement of the uvea. In spite of very careful examination beforehand by competent observers no signs of uveal disease were noted.

Conclusions

From the study of this small number of cases, it would appear that ACTH had no demonstrable effect in the reduction of intraocular pressure in primary glaucoma. On the other hand, the increased intraocular pressure accompanying anterior uveal disease showed an effective drop in tension and subsidence of the inflammatory process. It is suggested that, if ACTH or some derivative with its effect becomes more readily available, it may be useful in the differentiation between primary and so-called secondary glaucoma.

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We wish to express our thanks to Dr. Louis G. Welt of the Department of Internal Medicine, and Dr. J. R. Mote, Medical Director of the Armour Laboratories, for their kind advice and coöperation.

SUTURED CONTACT LENSES FOR CONTENTION OF THE GRAFT IN KERATOPLASTY

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Sutures inserted in the usual way, crossing over the graft, in keratoplasty never assure exact coaptation of the transplant to the recipient cornea. Also, their use is not without risk of injury to the superficial layers of the cornea. On the other hand, sutures inserted in the depth of the graft in order to assure direct fixation damage the corneal tissues and impose, even upon first-class operators, manipulations of real difficulty.

In order to avoid these difficulties, a new procedure for contention of corneal grafts has been adopted.

A contact lens which exactly covers the corneal area is sutured to the eyeball. The graft is thus maintained by capillary adhesion in exact appositon with the cornea. Moreover, the inner surface of the optically shaped shell (contact lens) so influences cicatrization as to improve the final visual results. This use of a contact lens is as applicable in superficial transplantations as in corneal grafting. Contact lenses may be used for round or square grafts; for transplants of a limited or total area of the corneal surface.

It has been surprising to note that the use of an optically shaped shell for contention of the graft is absolutely painless for the patient and harmless to the corneal tissues. Even after 15 days, the graft is not injured. This would tend to prove that the interchanges occurring on the outer face of the cornea are of moderate importance in relation to the metabolism through the depth of the stroma. This constitutes one of the main reasons for assuring perfect contact between the graft and recipient cornea.

First, the contact lens has to be fitted. A standard contact lens is perforated at the periphery by three narrow holes for the sutures. These holes are placed in position on the eye by means of colored spots (fig. 1). Silk sutures are passed through the holes and firmly fastened in the depth of the corneoscleral limbus (figs. 2 and 3). Shell and sutures are kept to one side so as not to interfere with the trephination of the cornea (fig. 4).

Fig. 1 (Fritz). Colored spots on the eye permit the exact placing of the contact lens sutures.

Fig. 2 (Fritz). Silk sutures are passed through the holes.

After the trephination is completed, the transplant set in place, and the corneal surfaces levelled (fig. 5), the contact lens is lowered over the graft which is held by capillary adhesion in close contact with the corneal surface (fig. 6). In order to equalize the traction of the three sutures, the slip-

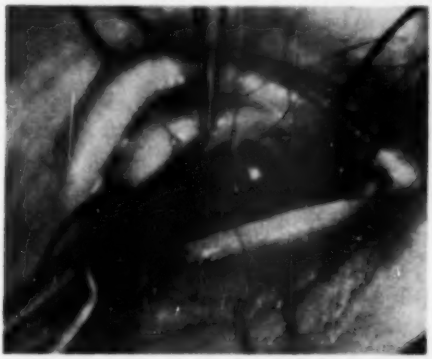

Fig. 3 (Fritz). The sutures are firmly fastened in the depth of the corneoscleral limbus.

Fig. 4 (Fritz). Shell and sutures are kept to one side so as not to interfere with the trephination.

knots are alternately tightened and with great care. The shell must be brought in close contact with the cornea without displacing the graft (fig. 7). Double knots are then tied and the eyelids are sutured.

When this technique is used, the corneal transplant is secure. Frequent dressings and

Fig. 5 (Fritz). After the trephination, the transplant is set in place and the corneal surfaces are levelled.

Fig. 6 (Fritz). The contact lens is lowered into place.

Fig. 7 (Fritz). The shell must be brought into close contact with the cornea without displacing the graft.

Fig. 8 (Fritz). When the contact lens is removed, 10 or 12 days later, coaptation of the outer surfaces of the graft and of the recipient cornea is perfect.

repeated instillation of drugs may be done without danger.

No exudates are formed between the contact lens and the graft, and both the graft and the anterior chamber remain visible. A mucoid exudate is formed around the shell and tends to prevent infection of the graft. No chemosis and no swelling of the eyelids develop, and the conjunctiva is not particularly congested.

When, 10 or 12 days later, the contact lens is removed, the corneal epithelium appears to be in good condition and coaptation of the outer surfaces of the graft and of the recipient cornea is perfect (fig. 8). In order to complete the optical shaping of the grafted cornea, a standard, flexible contact lens may be used to maintain a light pressure until cicatrization is complete.

SUMMARY

In keratoplasty, the best optical cicatrization is obtained by the use of the sutured contact lens to maintain close contact between the graft and the recipient cornea.

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NONDIABETIC LIPEMIA RETINALIS

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In lipemia retinalis the appearance of the retinal vessels depends upon the presence of an excessive concentration of neutral fat in the blood.[1,2] Other lipids (cholesterol, cholesterol esters, and phospholipid) also may be present in abnormally high concentration, but they are incidental and do not contribute to the ophthalmoscopic picture.

It has been noted that lipemia retinalis appears when the total blood fats exceed 3.5 percent, and disappears when these fats become less than 2.5 percent.[3] The exact level of neutral fat in the blood, above which plasma is sufficiently turbid to become visible in the retinal vessels, to our knowledge has not been accurately determined.

Since the condition was first described and named by Heyl,[4] in 1880, approximately 70 cases have been reported in the literature. Most of the patients were persons afflicted with diabetes mellitus.

A small number of cases have been reported in which lipemia retinalis has occurred in the absence of diabetes mellitus: Wagener,[5] in 1922, reported on a 9-year-old nondiabetic boy suffering from lymphatic leukemia in whom lipemia retinalis developed two weeks after radiation therapy. Total blood fats were estimated at five percent.

Holt, Aylward, and Timbres,[6] in 1936, described two patients, aged 11 and 2½ years, nondiabetic, with hepatosplenomegaly and totals for blood fats of 7.0 and 3.0 percent, respectively. The authors postulated

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that they were dealing with an anomaly of lipid metabolism analogous to Gaucher's or Niemann-Pick disease. In a later article (1939)[7] they suggested that this condition seemed to be familial.

Kauffman,[8] in 1943, described a nondiabetic 25-year-old colored man with hypertension, alcoholism, chronic gastritis, and transient lipemia retinalis.

Lepard,[6] in 1944, reported the condition of a 6-year-old nondiabetic boy with hepatosplenomegaly and lipemia retinalis which was readily detectable when the patient was maintained on a high-fat diet.

Grossman and Hitz,[1] in 1948, reported on a 55-year-old man in whom diabetes had been excluded, who had an enlarged liver, and marked lipemia retinalis.

We wish to report three cases in which nondiabetic lipemia retinalis was encountered at the Mayo Clinic during recent years.

Report of cases

Case 1

History. A white man, aged 59 years, while bringing his wife to the clinic for treatment, decided to undergo a general physical examination himself. He had no complaints. He stated that he preferred fatty foods, smoked an average of 15 cigars a day, and did not use alcohol. His weight was 169 pounds, his height 65 inches. Systolic blood pressure was 105 mm. Hg and diastolic 75 mm. Hg. The liver and spleen were not palpable. The skin was tanned, smooth, slightly oily, and free from eruptive lesions. There was no clinical evidence of acidosis.

Eye examination. Vision of the right eye was 6/15, and of the left, 6/6. There was low myopia of the right eye. On routine examination of the ocular fundi we were surprised to find the picture of mild lipemia retinalis: the arterioles appeared widened and somewhat ribbonlike, their light reflex diffused and softened, their color lightened to a pale, salmon pink. The veins likewise appeared widened and flattened, their color a light rose. These changes were most pronounced in the smaller branches, diminishing toward the disc.

Laboratory studies. The specific gravity of the urine was 1.006; the reaction, acid; sugar and albumin were not found. Hematologic studies revealed 4,640,000 erythrocytes and 7,400 leukocytes per c.mm. of blood; the value for hemoglobin was 14.6 gm. per 100 cc.; the sedimentation rate was 16 mm. in one hour; result of the Kline test was negative; the value for fasting blood sugar was 103 mg. per 100 cc. of blood. Values for fasting plasma lipids were as follows: total lipids, 3,584 mg.; cholesterol, 640 mg.; and fatty acids, 2,944 mg. per 100 cc. of plasma. (The normal ranges for these factors in our laboratory procedures are: total lipids, 400 to 650; cholesterol, 150 to 250; and fatty acids, 250 to 400, expressed in mg. per 100 cc. of plasma.) Tests of hepatic function were attempted by means of the dye-retention method, but were not completed because the gross milky and opaque condition of the serum precluded accurate colorimetric readings.

This patient's hyperlipemia, confirmed by results of laboratory studies as well as by the gross appearance of the serum, could be ascribed to no known cause. After the patient had been maintained for two days on a low-fat diet, the retinas no longer presented visible evidence of lipemia and the ocular fundi were normal. The patient was unwilling to remain for additional studies.

Study of son. At our suggestion, the patient's son, an only child, presented himself for examination. He was 35 years of age, weighed 225 pounds, was 70 inches in height, and considered himself to be in good health. Results of the physical examination were essentially negative, liver and spleen were not palpable, and the skin was smooth and slightly oily. The ocular fundi were normal in appearance.

Studies of the urine and basal metabolism gave normal results. The value for fasting blood sugar was normal and electrocardiographic procedure gave negative results; however, the laboratory reported that grossly the blood serum was creamy and opaque, and that the value for total plasma lipids was 1,872; for cholesterol, 268; for cholesterol esters, 162; for phospholipids, 432; and for fatty acids, 1,604, expressed in mg. per 100 cc. of plasma. A low-fat diet was instituted for the patient, and five days later the value for total plasma lipids had decreased to 1,164 mg.; for cholesterol, 254; and for fatty acids, 910 mg. per 100 cc. of plasma.

Case 2

History. A 33-year-old white man was admitted to a hospital for restraint and for examination; his history was one of social inadequacy, nervousness, and instability, becoming progressively worse over a 10-year period, with increasing recourse to alcohol. For a year or two prior to his admission he had consumed an average of 2 or 3 quarts of beer each day, with occasional drinks of whiskey in addition. The intake of food had been irregular. Thyroidectomy performed a year previously produced only brief subjective improvement and gain in weight.

Examination disclosed a 6-foot, 147-pound, mildly agitated man whose breath was alcoholic; the blood pressure was 114 mm. Hg, systolic and 64 mm. Hg, diastolic. There were a healed thyroidectomy scar, and tenderness in the left epigastrium. The liver and spleen were not palpable; the skin was smooth and free of xanthomas.

Eye examination. The ocular fundi revealed intense lipemia retinalis, the vessels appearing essentially white, the discs a gray, waxy color.

Laboratory studies. Results of laboratory studies, including the Kline test, urinalysis, erythrocyte, and leukocyte count, glucose tolerance test, and values for serum proteins, blood sugar and carbon-dioxide combining power, all were essentially normal. However, it was noted that the blood serum was grossly milky, and for this reason the hepatic function test by the dye-retention method was not done.

Determinations of serum lipids at that time gave the following values: total lipids, 4,740; cholesterol, 1,212; cholesterol esters, 792; lecithin, 1,136; fatty acids, 3,528, expressed as mg. per 100 cc. of plasma. The differential blood smear showed moderate hypochromasia with increased regeneration; sternal puncture revealed an increase in lipid material, marked increase in monocytes and reticulo-endothelial components, many of the latter possessing large vacuoles which almost completely filled the cytoplasm, and were interpreted as being suggestive of lipid histiocytosis.

After four days of hospitalization of this patient on a high-carbohydrate, high-vitamin intake, the condition of the fundi returned to normal. Serum lipid studies at that time gave values as follows: total lipids, 1,700; cholesterol, 628; cholesterol esters, 422; lecithin, 556; fatty acids, 1,032, expressed as milligrams per 100 cc. The patient was dismissed with the diagnosis of "psychopathic personality, chronic alcoholism, and lipemia of unknown cause."

Case 3

History. A 7-month-old white male infant was brought to the hospital for treatment of anorexia; the diagnosis of Niemann-Pick disease had been made elsewhere. At four months of age, fever and cough had developed, as a result of bronchopneumonia, which resolved on four days' hospitalization and penicillin therapy. At five months of age splenomegaly had been noted; and a specimen of blood drawn when the child was six months old had been described to the parents as being "milky-orange."

On examination of the infant, the spleen was found to be enlarged three fingerbreadths below the costal margin; the liver was palpable two fingerbreadths below the costal margin. There were several small, flat, yellow papules in the skin about the face and forehead.

Ophthalmoscopic examination disclosed pronounced lipemia retinalis, the large retinal vessels near the disc were creamy purple, blending to a grayish white of the smaller vessels. It was difficult to distinguish arteries from veins.

Laboratory studies. Results of urinalysis and erythrocyte and leukocyte counts were noncontributory. The blood serum had a milky color. The value for total serum lipids was 5,242 mg. per 100 cc.; that for plasma cholesterol was 448 mg. per 100 cc. Blood smears showed an increase in monocytes, and bone marrow obtained by sternal puncture showed many reticulo-endothelial cells, with increased storage of fat. The child was dismissed with the prescription of a low-fat diet, with a clinical diagnosis of "Niemann-Pick disease."

Comment

Any explanation of nondiabetic lipemia retinalis must remain speculative because of the present lack of understanding of many of the aspects of the absorption, transportation, and utilization of fat. Several possible explanations of lipemia are: (1) Excessive absorption of neutral fat from the bowel, (2) excessive mobilization of neutral fat from the tissues, and (3) slow removal of neutral fat from the blood. Which factor or combination of factors is responsible, it is not possible to say.

Summary

Lipemia retinalis occurs but rarely in nondiabetic persons. We have reported herein three cases. One patient was a man who presented the picture of idiopathic hyperlipemia, one was a man who was a chronic alcoholic, and one was a male infant who was afflicted with Niemann-Pick disease.

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THE EFFECTS OF MICROWAVE DIATHERMY ON THE EYE*

An Experimental Study

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Microwaves, which are continuously generated by the multicavity magnetron tube and which have been used in the recently developed microwave diathermy, can be reflected, refracted, and diffracted. They also can be concentrated by a suitable type of corner reflector into a narrow beam. These physical characteristics make microwaves particularly suited for heating relatively small regions of the body, without unduly raising the temperature of nearby structures. Unlike short-wave and long-wave diathermy, microwave diathermy lends itself to a definite localization of heating.

In this study the effects of microwave diathermy on intact as well as on enucleated eyes of dogs were investigated. This study was done in order to determine the changes in the temperatures of the orbital tissues and aqueous and vitreous humors of the eye after exposure to microwaves. Different distances of the microwave director from the eye surface, various durations of exposure to microwaves and different power outputs of the generator were used in an attempt to establish a dose of microwaves which would not damage the eye. Furthermore, ophthalmoscopic studies were made on the eyes before and after exposure to microwaves; after enucleation, histologic sections and microscopic examination of the eyes were made in order to note the pathologic changes produced in the eye and to determine distances, durations, number of exposures, and amount of microwave energy causing these changes.

Considerable experimental work has been done on the effects of long-wave and short-wave diathermy on the eye. In 1932, Moncreiff, Coulter, and Holmquest[1] studied the heating effect of short-wave diathermy on the eye. In order to measure temperature of the conjunctiva, anterior chamber, vitreous body, and orbit they used thermocouple needles as large as lumbar-puncture needles, which were left in place during exposure of the eyes of 40 anesthetized dogs to diathermy waves. They stated that by means of diathermy currents of intensities which appeared to be within the limits of safe clinical application—namely, the application of diathermy currents of 600 ma. for 15 minutes—average maximal temperature elevations of 4.49°C. in the orbit, 6.98°C. in the cavum oculi, and 7.11°C. in the conjunctiva were produced. In a comparative study of the thermal effects of diathermy, infrared radiation and electric heating pads on the eye and orbit, the same authors[2] reported that even in the anterior zones of the eye the heating power of diathermy is greater than that of infrared radiation and much greater than that of the heating pad.

Kokott[3] observed that the application of six-meter diathermy waves to the eyes of rabbits for 15 minutes heated the vitreous about 3°C. and caused damage to the nearby skin. By histologic examination of the eyes of cats which had been exposed to large doses of seven-meter diathermy waves, Plitas[4] noted damage to the retina and optic

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nerve. He concluded that these ocular structures were most susceptible to the action of short waves.

By a long series of irradiations of the eyes of rabbits with short waves, Scheyhing[5] produced superficial corneal clouding and marginal ulcers of the lids, which healed with scarring. Kiewe[6] reported that after exposure of the rabbit's eye to seven-meter short waves, the temperature rise was greatest at the posterior pole and decreased gradually toward the anterior segment of the eye.

Puntenney and Osborne[7] found that within one minute after 10-minute exposures of the eyes of 11 narcotized dogs to six-meter short waves, the average temperature of the vitreous was 109°F., of the subconjunctiva 106.6°F., and of the orbit 104°F. From photographs of the ocular fundus of dogs made before and after exposure of the eyes to six-meter waves, the authors concluded that neither vasoconstriction nor vasodilatation of the retinal vessels occurred during exposure. Histologic examination of the eyes which had been enucleated on the 7th to 14th day after exposure to six-meter waves revealed cutaneous burns of the lids, swelling of the scleral and ciliary nerves, separation of the internal limiting membrane of the retina, edema of the corneal stroma, and slight posterior subcapsular swelling of the lens.

There is hardly any detailed study of the effect of microwaves on the eye. In a recent report, Osborne and Frederick[8] found that exposure of the eye to microwaves when using 60 to 80 percent of the maximal output of the Raytheon portable microwave generator, with the "C" director at a distance of two inches (about five cm.) from the skin, for a period of 20 minutes, raised the temperature of the vitreous to an average of 105°F. The first temperature measurements were taken within one minute and a half after exposure to microwaves. They stated that repeated exposure of one eye of one dog to microwaves, using the same technique of application for six times over a period of three weeks, did not produce any damage in the eye other than a temporary conjunctival injection at the end of each exposure.

Methods

The microwave generator used in this study was an experimental model of the microtherm containing an air-cooled multicavity magnetron tube which generates microwaves at a frequency of 2,450 megacycles per second, corresponding to a wave length of about 12 cm. The energy was transported from the generator to the director through a coaxial cable. Director "C,"[9] the corner-reflector type, was used exclusively in this study on the eye because the surface heat pattern of this director is confined to a relatively small oval area with maximal heating in the center of the pattern.

The temperatures were recorded galvanometrically by means of copper constantan thermocouples mounted in fine hypodermic needles (no. 25). The deflections of the galvanometer were either read directly from the scale on a screen or continuously recorded on a moving photographic film throughout the experiment.

In one series of experiments in which 36 dogs were used, the temperatures of the aqueous and vitreous humors and of the deep tissues in the orbit were recorded before and after exposure of the eye to microwaves. To insure uniformity, the following procedure was carried out in each experiment. The animal was anesthetized with pentobarbital sodium given intravenously (25 mg. per kilogram of body weight). More anesthetic was administered when needed. To stabilize the eye without causing disturbance of the electromagnetic field, nonmetallic supports were used to immobilize the head of the dog. A plastic tube was introduced into the trachea to maintain a free intratracheal airway.

Silk sutures were passed through each of the eyelids to hold the lids open and through the nictating membrane to pull it away from the anterior surface of the eye. Also, silk

sutures were placed in the cornea at the limbus at the 6- and 12- o'clock positions in order to immobilize the eye during exposure to microwaves and to stabilize it during the insertion of the thermocouple needles.

After exposure of the sclera by excision and reflection of the conjunctiva from the upper temporal corneal limbus, a small scleral incision was made, through which the thermocouple needle was introduced into the vitreous. One thermocouple was inserted into the orbit through the conjunctiva near the inner canthus. Another thermocouple was inserted directly into the aqueous at the corneal limbus. In order to prevent damage to the eye the thermocouples were carefully supported and held firmly in place by clamps which prevented any change in position of the needles in the aqueous and vitreous.

After control temperatures had been established, the thermocouple needles were carefully withdrawn. The director was aimed at the cornea and was accurately spaced from the corneal surface. The distance from the cornea to the center of a plane joining the most anterior metal edges of the director was measured. The microwave generator was then turned on and the output was kept constant by manipulating the variac as needed. After irradiation of the eye, the thermocouple needles were quickly reinserted to their respective positions as in the control determinations. To allow time for the introduction of the needles and for the thermocouples and galvanometers to come into equilibrium, the first readings were taken exactly one minute after discontinuation of the heating. The temperatures were continuously recorded for about one half hour after the microwaves had been turned off.

In order to determine the optimal dose for the production of safe elevations of temperature in the eye without damage to the eye structures, a number of experiments were performed using six different methods of exposing the eye to microwaves with different outputs, different distances of the cornea from the director, and different durations of exposures. These various factors are listed in Table 1.

TABLE 1

AVERAGE TEMPERATURES IN THE EYES OF ANESTHETIZED DOGS BEFORE, AND ONE MINUTE AFTER, EXPOSURE TO MICROWAVES

Experiments	Generator Output		Distance of Director (inches)	Duration of Exposure (minutes)	Average Temperature (degrees centigrade)								
					Orbital Tissues			Vitreous Humor			Aqueous Humor		
	%	Watts			Before	After	Difference	Before	After	Difference	Before	After	Difference
5	75	94	5	30	37.2	38.1	0.9	37.3	40.1	2.6	36.9	38.9	2.0
16	75	94	3	30	37.4	39.3	1.9	37.6	40.8	3.2	37.0	39.8	2.8
11	75	94	3	20	38.0	38.9	0.9	37.0	39.6	2.6	37.2	39.6	2.4
10	75	94	3	10	37.5	38.2	0.7	36.8	39.0	2.2	36.9	39.2	2.3
11	75	94	7	30	38.3	41.1	2.8	38.1	43.8	5.7	37.5	41.8	4.3
9	98	122	1½	30	37.8	40.8	3.0	36.9	43.8	6.9	37.2	42.0	4.8

RESULTS

Effects of microwave diathermy on the temperature of the aqueous, vitreous, and orbit. In every experiment in this study the actual temperatures of the vitreous and aqueous after exposure of the eye to microwaves were consistently higher than that of the deep orbital tissues; and in most of the experiments, the temperature of the vitreous was higher than that of the aqueous. However, when the duration of exposure was 10 minutes, the average temperature of the aqueous was slightly higher than that of the vitreous. In every instance, the elevation in temperature of the aqueous and of the vitreous exceeded that of the deep orbital tissues.

In five experiments, using 75 percent of the output of the microwave generator with

the director at a distance of five inches (about 13 cm.) for 30 minutes, the average temperatures one minute after exposure to microwaves were 38.1°C. for the deep orbital tissues, 40.1°C. for the vitreous, and 38.9°C. for the aqueous. In this series, the average rise in temperature of the deep orbital tissues was 0.9°C., with a range of 1.6° to 0.8°C.; that of the vitreous was 2.6°C., with a range of 3.2° to 1.6°C.; that of the

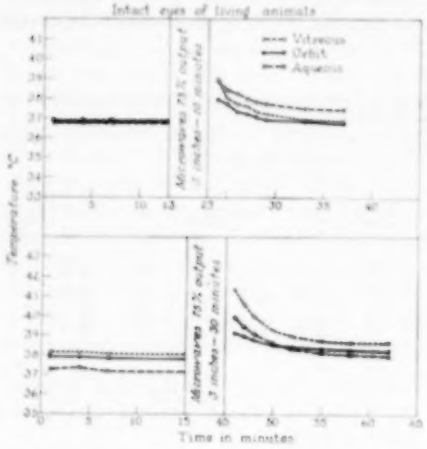

Fig. 1 (Daily, *et al.*). Temperature curves of deep orbital tissues, vitreous, and aqueous of the eyes of anesthetized animals before and after exposure to microwaves.

aqueous was 2.0°C., with a range of 2.9° to 1.0°C. (table 1).

In 16 experiments using 75 percent of the output of the microwave generator, with the director at a distance of three inches (about eight cm.) for 30 minutes, the average temperatures one minute after exposure were 39.3°C. for the deep orbital tissues, 40.8°C. for the vitreous, and 39.8°C. for the aqueous. In this series, the average rise in temperature of the deep orbital tissues was 1.9°C., with a range of 2.6° to 1.1°C.; that of the vitreous was 3.2°C., with a range of 4.2° to 2.1°C.; and that of the aqueous was 2.8°C., with a range of 3.4° to 1.4°C. (table 1).

In 11 experiments using 75 percent output with the director at a distance of three inches for 20 minutes, the average temperatures one minute after exposure to microwaves were 38.9°C. for the deep orbital tissues, 39.6°C. for the vitreous, and 39.6°C. for the aqueous. In this series, the average rise in temperature of the deep orbital tissues was 0.9°C., with a range of 1.8° to 0.3°C.; that of the vitreous was 2.6°C., with a range of 4.0° to 2.0°C.; and that of the aqueous was 2.4°C., with a range of 3.8° to 1.2°C. (table 1).

In 10 experiments using a 75 percent output with the director at a distance of three inches for 10 minutes the average temperatures one minute after exposure were 38.2° C. for the deep orbital tissues, 39.0°C. for the vitreous, and 39.2°C. for the aqueous. In this series, the average rise in temperature of the deep orbital tissues was 0.7°C., with a range of 1.6° to 0.2°C.; that of the vitreous was 2.2°C., with a range of 3.3° to 0.9°C.; and that of the aqueous was 2.3°C., with a range of 4.4° to 0.8°C. (table 1).

In 11 experiments using 75 percent output with the director at a distance of two inches (about five cm.) for 30 minutes, the average temperatures one minute after exposure were 41.1°C. for the deep orbital tissues, 43.8°C. for the vitreous, and 41.8°C. for the aqueous. In this series, the average rise in temperature of the deep orbital tissues was 2.8°C., with a range of 3.6° to 1.6°C.; that of the vitreous was 5.7°C., with a range of 8.6° to 4.1°C.; and that of the aqueous was 4.3°C., with a range of 6.6° to 2.9°C. (table 1).

In nine experiments using 98 percent output with the director at a distance of 1.5 inches (about four cm.) for 30 minutes, the average temperatures one minute after exposure were 40.8°C. for the deep orbital tissues, 43.8°C .for the vitreous, and 42.0°C. for the aqueous. The average rise in temperature of the deep orbital tissues was 3.0°C., with a range of 3.6° to 2.4°C.; that of the vitreous was 6.9°C., with a range of

9.4° to 4.2°C.; and that of the aqueous was 4.8°C., with a range of 7.2° to 2.8°C. (table 1).

An interesting observation is the rate and degree of cooling of the eye after exposure to microwaves. After the cooling curves had been recorded it was observed that, in many of the eyes, the temperatures did not return to control values but formed a new base line above the original level (fig. 1). This might be explained by the observation that in these animals there was a general rise in the temperature of the body after exposure to microwaves.

In all the experiments, plateauing of the cooling curve was practically complete within 15 minutes after discontinuation of heating, and much sooner in the experiments in which there was relatively little rise in temperature following exposure to microwaves (fig. 1). As a rule, at the end of 20 minutes after exposure to microwaves, the temperature of the aqueous was lower than that of the vitreous or deep orbital tissues.

TABLE 2

MARKED DIFFERENCE IN EFFECTS OF MICROWAVES* ON THE TEMPERATURE OF THE INTACT EYE IN THE LIVING ANIMAL AS COMPARED WITH THAT IN THE DEAD ANIMAL

Condition of Animal	Temperature Rise (degrees centigrade)		
	Orbit	Vitreous	Aqueous
Alive	0.8	1.9	1.6
Dead	3.1	6.8	6.7

* The generator output was 75 percent (94 watts); distance of director, 3 inches (about 8 cm.); and duration of exposure, 20 minutes.

The rapid rate of cooling of the vitreous and aqueous was striking, since both of these media are entirely avascular. Evidently most of the heat produced in these structures as a result of exposure to microwaves was carried away by the blood circulating in the vascular tunics adjacent to them. To substantiate this explanation, a number of experiments were performed in which intact eyes of living animals, and the contralateral intact eyes of the same animals immediately after death, were exposed to the same dose of microwaves under identical conditions. The results are illustrated in Figure 2. After exposure to microwaves, the rises in temperature of the aqueous and the vitreous of the intact eye of the living animal were much lower than those of the intact contralateral eye of the same animal after death (table 2). This proved to us that the blood circulating in the vascular tunics adjacent to the aqueous and vitreous efficiently carries away a large part of the heat produced in these media by exposure to microwaves.

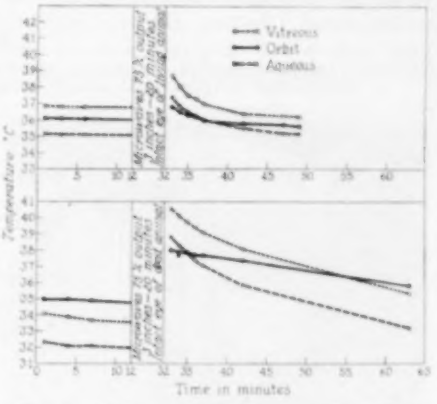

Fig. 2 (Daily, *et al.*). Difference in rise in temperature of the deep orbital tissues, vitreous, and aqueous of the intact eyes of the same animal, one before and one after death.

Clinical and pathologic changes in the eye after microwave diathermy. Another series of experiments was performed on eight dogs anesthetized as in the previous series. The right eyes were exposed to microwaves at specific output, fixed distance, and duration. The left eyes were used for controls. No records of temperature were made in this series. However, the eyes were examined clinically, including ophthalmoscopic examinations of the media and fundi, before and after each exposure to microwaves. The eyes of three of these animals were sectioned and studied histologically. The remaining

five animals are still under observation, and their eyes will be examined regularly for at least six months, after which they will be enucleated for microscopic study.

In this series of experiments care was taken that eyes exposed to microwaves were not touched. Since the cornea of the infraverted eye in the anesthetized dog is usually about two thirds covered by the lower lid and nictitating membrane, it was not possible to center the director by aiming at the pupil. Instead, the director was carefully aimed toward the center of the eyeball along a line through the upper limbus of the cornea. The cornea and anterior chamber were located in the center of the area of maximal heating. During exposure to microwaves, the lids were kept open by means of strips of adhesive tape. The duration of exposure of all eyes in the series was 30 minutes.

No clinically observable changes were noted in the eye of Animal 1 during or after a series of six exposures to microwaves, once every other day, using 75 percent output at a distance of five inches (about 13 cm.) (table 3). The eyes of this dog were enucleated 24 hours after the last exposure. No pathologic changes were seen in any of the histologic sections.

No clinically observable changes have been noted in the eyes of Animals 2 and 3 during or after repeated daily exposures 6 and 10 times, respectively, to microwaves, using 75 percent output at a distance of

TABLE 3

CLINICALLY OBSERVED EFFECTS OF REPEATED EXPOSURES OF THE EYES OF ANESTHETIZED DOGS FOR 30 MINUTES TO SPECIFIED OUTPUTS OF MICROWAVE GENERATOR AND VARYING DISTANCES OF DIRECTOR

Animal	Generator Output		Distance of Director (inches)	Exposures	Frequency of Exposures	Eye Findings
	%	Watts				
1	75	94	5	6	Once every other day	No clinically observable pathologic effects.
2	75	94	3	6	Once daily	No clinically observable pathologic effects to date. Animal is still under observation.
3	75	94	3	10	Once daily	No clinically observable pathologic effects to date. Animal is still under observation.
4	75	94	2	1		24 hours after the exposure, lower ¾ of cornea was cloudy and stained lightly with fluorescein; the pupil was semidilated and unreactive.
5	75	94	2	10	Once daily	No clinically observable pathologic effects to date.
6	75	94	2	8	Once daily	During period of repeated exposures, there was corneal clouding, and two dilated conjunctival vessels; 6 days after the last exposure, anterior cortical rosette cataract was observed. Posterior cortical cataract developed later. Animal is still under observation.
7	98	122	1½	2	Once daily	24 hours after exposure, corneal clouding and ulceration, semidilated unreactive pupil, elevation and whitening of retina about disk, and reddening of disk appeared.
8	98	122	1½	7	Once daily	During period of repeated exposures, there was corneal clouding and conjunctival injection; 24 hours after the last exposure, anterior cortical cataract developed. Posterior cortical cataract developed later. Animal is still under observation.

three inches (about eight cm.) (table 3). These two animals are still under observation and their eyes are examined regularly in order to determine whether any delayed changes may develop.

Clinically observable changes were seen in the eyes of Animals 4 and 6 after exposure to microwaves, using 75 percent output at a distance of two inches (about five cm.) (table 3). The right eye of Animal 4 was exposed only once for 30 minutes. Twenty-four hours later the following inflammatory signs were seen. The conjunctiva was intensely injected. The lower three fourths of the cornea (that part covered by the lower lid and nictitating membrane during exposure to microwaves) was of a dull, glazed appearance, and the corneal epithelium in this area stained lightly with fluorescein. The aqueous appeared somewhat cloudy. A three-percent solution of homatropine dropped into the eyes produced full mydriasis in the control eye and partial mydriasis in the eye that had been exposed to microwaves. The eyes were immediately enucleated and prepared for histologic study.

Before it was sectioned, the formalinized eye which had been exposed to microwaves did not show gross pathologic changes. In stained sections (hematoxylin and eosin) the pathologic changes were limited to the cornea and limbal region. The limbal blood vessels were dilated, and some fibrinous exudate was present on the anterior surface of the corneal epithelium. The cellularity of the substantia propria of the cornea was greater than normal. Some of these cells were infiltrating polymorphonuclear leukocytes.

One eye of Animal 6 was exposed to microwaves, using 75 percent output at a distance of two inches (about five cm.), once daily, eight times (table 3). Before the second exposure an area of faint clouding was seen in the upper part of the cornea. This clouding diminished and completely disappeared during the next seven days, even though the eye was exposed to microwaves once daily during this period. However, before the third exposure of the eye to microwaves, two dilated vessels became evident in the bulbar conjunctiva extending from above to the limbus of the cornea. These vessels remained prominent throughout the rest of the exposures but gradually diminished in size and disappeared in a few days after irradiation had been discontinued.

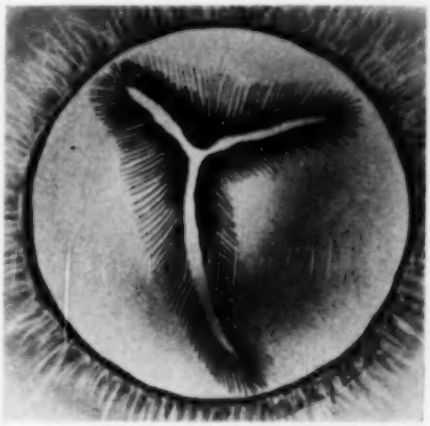

Fig. 3 (Daily, *et al.*). Drawing, as seen through the ophthalmoscope, of the anterior rosette cataract produced by repeated exposure of the eye to microwaves.

Six days after the last exposure to microwaves a faint anterior cortical cataract in the form of a rosette was first observed ophthalmoscopically. Daily observations revealed that the density and size of this rosette cataract increased markedly until, less than one week after it was first observed, it was seen by lateral illumination with a flashlight as an orange, glowing structure against the dark background of the lens. Ophthalmoscopically, it appeared as a dark silhouette against the brilliant golden tapetal reflex from the dog's fundus (fig. 3). With the hand slitlamp it was localized beneath the anterior capsule.

The cataract reached its maximal density in about two weeks after the last exposure to microwaves. For about two weeks there-

after, no obvious change was noted in its structure. From then on, the size and density of the cataract progressively diminished. The feathery opaque fibers decreased in number and the stemlike sutural opacity became narrower and spiderlike in appearance. Figure 4 shows the ophthalmoscopic appearance of the cataract during the initial stages of regression of the anterior cortical opacity.

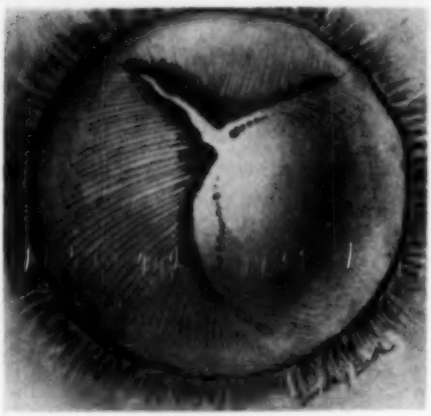

Fig. 4 (Daily, *et al.*). Drawing of the same cataract shown in Figure 4, as seen through the ophthalmoscope during its regression. Note the disappearance of a large portion of the opacity.

Eight weeks after it was first detected, this anterior cortical opacity was visible only as a thin, jagged, horizontal line across the pupillary area. At this time, opacification of the posterior part of the lens became noticeable. A number of small, orange-colored dots were visible on the posterior capsule by lateral illumination, and a faint, concave, white opacity and faint, sutural, orange, glowing opacities were seen in the posterior part of the lens in the region of the posterior pole.

In one week this posterior cortical opacity had increased in density and extent. The pigmented dots on the posterior capsule were no longer seen, but the cataract was more easily observed with a flashlight as a white, concave, three-cornered, shield-shaped structure enclosing Y-shaped dark suture lines. Ophthalmoscopically, this structure appeared only as an oval granular opacity through which fundus detail was visible.

One eye of Animal 5 was also exposed to microwaves, using 75 percent output at a distance of two inches (about five cm.), once daily, 10 times. In spite of the fact that it was exposed a greater number of times than Animals 4 and 6, no change was observed clinically (table 3). This animal had a long snout, and the director had to be aimed at the eye in a direction at right angles to the anteroposterior axis of the eyeball. It is possible that less microwave energy was directed into the eye of this animal. However, variation in resistance to microwave energy may be another factor.

Clinically observable changes developed in the eyes of Animals 7 and 8, which were exposed to microwaves, using 98 percent output at a distance of 1.5 inches (about four cm.) (table 3). One eye of Animal 7 was exposed once daily, two times. Twenty-four hours after the first exposure marked photophobia was evident and the following inflammatory reactions were observed. The conjunctiva showed moderately severe diffuse injection and mild chemosis. Corneal luster was markedly dulled. Ophthalmoscopic examination revealed fine vesicles in the cornea, but no definite opacities were observed in either the lens or the vitreous. The retina, particularly in the region near the disc, appeared to be whiter and thicker than that in the unexposed left eye, and the refractile spots in the tapetum had lost their sparkling reflexes. No retinal hemorrhages were seen and no definite differences could be detected between the size of the retinal vessels in this eye and in the unexposed left eye. The optic disc was much redder than that of the unexposed left eye, and its superior third, including the margin of the disc and the adjacent retina, was hazy.

Two days after the eye was exposed to microwaves for the second time, the inflammatory reactions were aggravated. Con-

junctival injection was intense and chemosis was increased. There was a large ulcer in the lower portion of the cornea adjacent to the limbus, and the remainder of the cornea had a ground-glass appearance. The aqueous and vitreous humors were very cloudy. The fundus could not be seen; only a yellow fundus reflex interrupted by stringy, black vitreous opacities was observed. The pupil did not contract when the dog was anesthetized as did the pupil of the unexposed eye. Both eyes were enucleated for pathologic study.

The pathologic findings on the exposed eye were as follows:

GROSS APPEARANCE. The gross diameters of the globe and cornea were within normal limits. There was a depression of the cornea between the 5- and 6-o'clock positions near the limbus. The corneal epithelium was roughened near the center. The entire cornea was cloudy. The anterior chamber had a small, dark mass behind the depressed area in the cornea. The rest of the anterior chamber appeared to be filled with opalescent material containing whitish, flocculent particles. After capping of the eye, the lens appeared firmly fixed in position and adherent to the iris. Faint cloudy streaks could be seen in the vitreous. The posterior portion of the retina showed many wrinkles. The optic disc was well demarcated and appeared elevated, with a tiny depression in the center.

MICROSCOPIC APPEARANCE. In the stained sections (hematoxylin and eosin) the corneal epithelium was edematous, some of the epithelial cells were swollen, and in some small areas the epithelium was detached from Bowman's membrane. In one area the epithelium was absent for two mm., and there were a few clumps of erythrocytes associated with a pink-staining fluid on the denuded surface (fig. 5). The fibers of the substantia propria were separated by numerous, rather elongated spaces of varying size, which appeared to be the result of edema, although the possibility that some of these spaces may have been due to artefact was not excluded. The substantia propria of the cornea also contained scattered polymorphonuclear leukocytes, and some erythrocytes near the limbus. On the posterior surface of the cornea were clumps of pigment, and in the region of the ligamentum pectinatum were phagocytes filled with pigment. In the lower part of the anterior chamber, fibrin, erythrocytes, leukocytes, and pigment-laden phagocytes were present

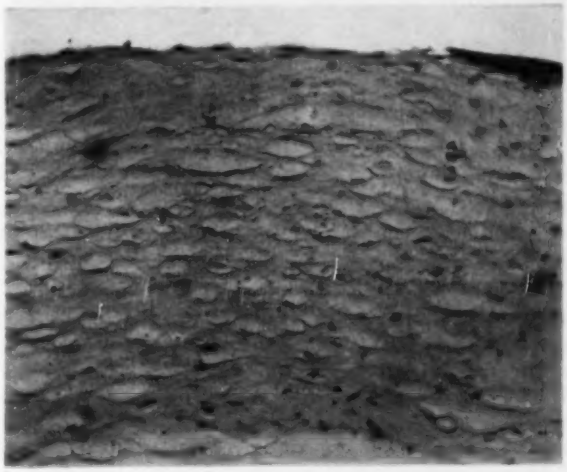

Fig. 5 (Daily, *et al.*). Cornea, showing area of loss of epithelium, and scattered infiltration of substantia propria with polymorphonuclear leukoyctes. The numerous spaces separating the fibers of the substantia propria appear to be due to edema (×65).

Fig. 6 (Daily, *et al.*). Lower part is a section of iris, showing hemorrhage, partial destruction of stroma, and disruption of posterior layer of pigmented epithelium; upper part is a hemorrhagic mass in anterior chamber, consisting chiefly of erythrocytes, fibrin, and macrophages filled with pigment (×75).

(fig. 6). The stroma of the iris was infiltrated with erythrocytes; there was some necrosis of the stroma of the iris and loss of most of the posterior pigment layer. The ciliary processes contained many erythrocytes. The ciliary body contained some erythrocytes just under the pigment epithelium. Except for one questionably degenerated spot near the equator, the lens did not show any definite pathologic change.

Below the optic disc, the choroid was markedly detached, and the subchoroidal space contained pink-staining exudate (fig. 7). Above the disc the choroid was slightly detached and the subchoroidal space contained delicate strands of pink-staining exudate.

Cystic degeneration was present in the retina. Pigment and phagocytes containing pigment were present in the nerve-fiber layer. The inner nuclear layer was thin, and the ganglion cells were reduced in number. The vitreous contained a very few erythrocytes and amorphous layers of pink-staining material resembling an exudate. The optic nerve did not show any definite pathologic changes.

The eye of Animal 8 which was exposed to microwaves, using 98 percent output at a distance of 1.5 inches (about four cm.), was irradiated once daily, seven times. Before the second exposure to microwaves, the eye showed the following inflammatory reactions. There was a mild, diffuse injection of the conjunctiva. The corneal luster was somewhat dulled. After the fifth exposure to microwaves, three small linear defects were detected in the cor-

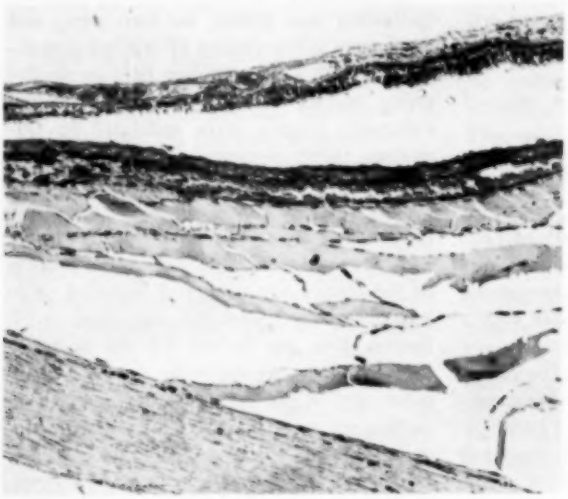

Fig. 7 (Daily, *et al.*). Section from posterior half of globe, showing extensive choroidal and subchoroidal exudate (×50).

neal epithelium near the center of the cornea by fluorescein stain. Grossly, the cornea appeared clear. One day after the last exposure to microwaves there was only one small, faintly staining defect in the corneal epithelium near the center of the cornea.

By ophthalmoscopic examination, a faint opacity was observed in the lens for the first time. This cataract at this time consisted of two straight lines which resembled an inverted V with an open apex. Daily observations of the cataract were made.

Within two days after the opacities were first seen, an additional line was present at the base of the inverted V, giving the opacity the shape of a triangle with open apices. The cataract progressed in size and density until within a week after it was first observed it had the ophthalmoscopic appearance seen in Figure 8. By lateral illumination with a flashlight, it, like the cataract previously described, was seen as an orange, glowing structure against the dark background of the lens. With the hand slitlamp, it was localized beneath the anterior capsule.

This cataract remained approximately unchanged for about two weeks, showing long feathery opaque fibers radiating from the dark suture lines. Then, like the other cataract, it regressed gradually, the dark suture lines became fainter and fainter, and the nasal side of the triangle completely disappeared. The appearance of the cataract at this stage is shown in Figure 9.

After one week, only the upper temporal edge of the cataract could be seen, and this was so faint in silhouette against the golden glow from the tapetum of the fundus of the animal that, had it not been carefully sought for, it would have been unnoticed.

About nine weeks after the anterior cortical opacity was first detected, opacification of the posterior part of the lens was seen for the first time. A concave, round, sharply circumscribed opacity was located in the inferior temporal quadrant of the posterior subcapsular cortex. By lateral illumination

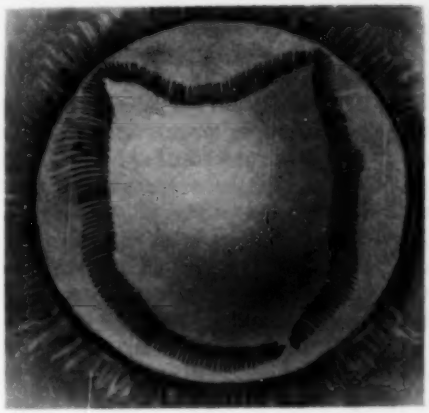

Fig. 8 (Daily, *et al.*). Drawing, as seen through the ophthalmoscope, of the anterior cortical sutural cataract produced by exposure of the eye to microwaves.

it appeared white but contained some dark areas. Ophthalmoscopically, it looked granular with a sharp, dark border. One week later the cataract appeared to extend from the posterior into the anterior cortex in the inferior temporal quadrant of the lens.

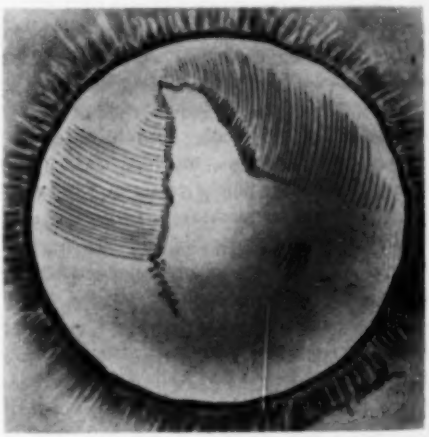

Fig. 9 (Daily, *et al.*). Drawing, as seen through the ophthalmoscope, of the same cataract shown in Figure 8, during its regression. Note the practically complete disappearance of the lower portion of the opacity.

Comment

If a certain range of dosage of microwaves, which does not damage the eye, can be found, microwave diathermy may provide a useful method for producing therapeutic elevations of temperature in the eye. The waves are focused by director "C" so that most of the heat produced is localized to a small region in the tissues. This allows efficient heating of small organs such as the eye without undue heating of the surrounding structures.

On the other hand, this study demonstrates that microwaves can damage the eye if dosage is not carefully managed. Damage can even result from only one exposure. One or all of the ocular structures may become acutely inflamed. However, repeated exposures over a period of days or weeks may cause injury if the distance, duration, and amount of microwave energy are not carefully controlled. The cataracts which developed in the eyes of two dogs after repeated exposure to microwaves are a good example of such damage.

Why lens opacities were not accompanied by extensive visible changes in the intraocular structures after repeated exposure of the eye to a high concentration of microwave energy is not clear. It is possible that the lens reaches a higher temperature than any of the other intraocular structures during exposure of the eye to microwaves. We have shown that the aqueous and vitreous reach a higher temperature than the deep orbital tissues; presumably, this is because they are avascular and must depend on the circulation in surrounding structures to dissipate the heat. The lens is a solid avascular body, surrounded mostly by avascular structures by means of which heat loss is relatively inefficient. Therefore, a higher temperature might develop in the lens than in other intraocular structures because it is relatively isolated from circulating blood.

The structure of the cataracts produced by exposure to microwaves is of interest. Both cataracts consisted of linear sutural opacities from which opaque feathery fibers of the lens radiated. Both cataracts first developed in the anterior cortex of the lens just beneath the capsule. One was a typical rosette cataract.

At a later date, posterior cortical opacities appeared in the lenses of the exposed eyes of both dogs. These cataracts resembled the early lens opacities which have been reported to occur after exposure of the eyes of pigmented rabbits to infrared radiation.[9] Infrared cataract, which has been encountered as an occupational disease in glass blowers and puddlers, is typically a posterior polar opacity and involves the posterior subcapsular cortex or, less frequently, the nucleus of the lens.[9]

One of the causes of anterior cortical rosette cataract is contusion of the globe.[10] One might suspect that one of these animals might have undergone accidental contusion of the globe. However, no evidence of contusion or trauma could be noticed; and the presence of the cataracts only in the eyes which were exposed to microwaves, and their absence in the contralateral control eyes, rules out contusion as the cause in this case. The appearance of the cataracts beneath the anterior capsule may be due to injury to the subcapsular epithelium which would interfere with the metabolism of the lens. However, the anterior capsule itself remained clear.

Reversible lens opacities are not in themselves remarkable, but the ability of the lens to recover from injury caused by repeated exposure to microwaves is worthy of comment. Why the anterior cortical opacification should be reversible is not understood. Cortical cataracts produced in the eyes of pigmented rabbits by exposure to infrared radiation have been reported to resemble rosette-shaped traumatic cataract in that they have a tendency to disappear.[11]

The rapid cooling of the vitreous after exposure to microwaves was of interest to us, in view of its avascularity. The lesser rise in the temperature of the vitreous of the

intact eye of the living animal as compared with that of the vitreous of the contralateral intact eye after death of the animal demonstrates the ability of the circulating blood in the tissues which partly surround the vitreous to carry heat away from the vitreous effectively.

It should be emphasized that the temperatures measured one minute after exposure of the eye to microwaves are not the maximal temperatures reached in the aqueous and vitreous during exposure to microwaves. A glance at the slope of the cooling curves (fig. 1) during the second minute after exposure to microwaves indicates that the temperatures have undoubtedly been falling comparatively rapidly during the first minute after exposure.

The curves indicate that the greater the temperature rise during heating, the more rapid is the fall after the heating is stopped. Consequently, any conclusions which may be drawn as to the safety of a stated dose and technique of application of microwaves to the eye are better judged by the absence of pathologic changes than by the magnitude of the rise in the recorded temperatures.

The two eyes that were repeatedly exposed to microwaves using 75 percent of the output of the generator with the director at a distance of three inches (about eight cm.), for a period of 30 minutes, so far show no clinically observable pathologic findings. Two of the three eyes that were repeatedly exposed to microwaves using the same plate current, and for the same period of time, but with the corner director at a distance of two inches (about five cm.), only one inch closer, showed pathologic changes.

Further study should be made before any opinion can be expressed as to the therapeutic possibilities of microwave diathermy in eye disease.

Summary

In order to determine the changes in temperatures of the orbital tissues, aqueous, and vitreous humors after exposure of the eye of the dog to microwaves, and to determine the pathologic changes in the eye resulting from exposure to microwaves, a study was made of the effects of various durations of exposure of intact as well as enucleated eyes at different distances, durations, and power outputs.

One series of acute experiments was performed on 36 dogs anesthetized intravenously with pentobarbital sodium (25 mg. per kilogram of body weight). Thermocouple needles were introduced into the orbit, aqueous, and vitreous humors of the eye and the temperatures were recorded before and after exposure to microwaves. The cooling curves were followed for about one-half hour after the microwaves were turned off.

Exposure of the eye to microwaves using 75 percent of the output of the generator with the corner director at a distance of three inches (about eight cm.) for 30 minutes produced an average temperature rise of 1.9°C. in the orbit, 3.2°C. in the vitreous, and 2.8°C. in the aqueous, exactly one minute after the microwaves were turned off.

Another series of experiments was performed on eight dogs similarly anesthetized, and their eyes were exposed to microwaves at specific output, fixed distance, and duration. No records of temperature were made in this series. However, the eyes were examined clinically, and ophthalmoscopic examinations of the media and fundi were made before and after exposure to microwaves.

The eyes of two animals that were repeatedly exposed, 6 and 10 times, respectively, to microwaves using 75 percent of the output of the generator with the corner director at a distance of three inches (about eight cm.) for 30 minutes, so far have shown no clinically observable pathologic findings.

Eight exposures of the eye of one animal to microwaves once daily for 30 minutes, using 75 percent output of the generator with the corner director at a distance of two inches (about five cm.), produced ophthalmoscopically observable anterior cortical

cataract within six days after the last exposure.

Seven exposures of the eye of another animal to microwaves once daily for 30 minutes, using 98 percent output with the director at a distance of only 1.5 inches (about four cm.), produced ophthalmoscopically observable anterior cortical cataract within 24 hours after the last exposure. Over a period of about nine weeks both of these anterior cortical cataracts increased in size and density and then regressed, and posterior cortical cataracts developed.

In one animal one exposure of the eye for 30 minutes to microwaves, using 75 percent output with the director at a distance of two inches (about five cm.), produced corneal clouding and partial iridoplegia within 24 hours after exposure. Microscopic examination of stained sections of this eye revealed that there was infiltration of the corneal stroma with polymorphonuclear neutrophils.

Similar clinical and histologic changes were produced in the eye of another animal within 24 hours after two exposures of 30 minutes each to microwaves, using 98 percent output with the director at a distance of 1.5 inches (about four cm.) and, in addition, vitreous opacities, reddening of the optic disc, whitening and elevation of the retina in the region of the disc were observed ophthalmoscopically. Microscopic examination of stained sections of this eye in addition revealed erythrocytes, leukocytes, and fibrinous exudate in the anterior chamber with hemorrhage into the iris and ciliary processes. Necrosis of the stroma of the iris and disorganization of the pigment layer of the iris, and subchoroidal exudate and cystic degeneration of the retina were also observed.

The Mayo Clinic.

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TOXOPLASMOSIS*

Diagnosis and Treatment

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You know that I am not an ophthalmologist by profession, and I hope that you will be charitable when I slip in some of my ophthalmologic descriptions. However, I have been studying toxoplasmosis since 1935, on and off, and have had an opportunity to collaborate with many ophthalmologists during those years. Thus, I have come to appreciate the problems which they encounter when it is necessary to decide whether or not certain manifestations in patients are or are not due to toxoplasmosis. My present discussion, therefore, will deal chiefly with those problems in toxoplasmosis which are of special interest in ophthalmologic practice.

Infection in Nature

Let me begin by saying that according to the most critical evaluation of the present evidence, Toxoplasma occur in nature only in a limited number of animals. We have no evidence that they are widespread or even occur in paddybirds, sparrows, lizards, or all sorts of other living beings so often listed in the literature. I should say that those records in the literature are based on morphologic examinations without the experimental support which I believe to be necessary for initial identification of a given parasite as Toxoplasma. One must be able to prove that a morphologically similar parasite is capable of producing disease in a variety of experimental animals—mice, guinea pigs, rabbits, chick embryos, monkeys. Unless one can demonstrate this pathogenicity for many hosts, one cannot speak of the parasite as Toxoplasma. There are a number of other protozoan parasites in birds and other animals, particularly the hemogregarines, which morphologically may simulate Toxoplasma. I will give you my own present opinion regarding the natural reservoirs from which human beings may acquire Toxoplasma.

Foremost in this respect are the domestic animals, especially the dog and cat. There is good evidence to suggest that the Toxoplasma can come out in their feces and urine. Contamination of a person's hands, with subsequent transmission of the parasites to the mouth, can constitute at least one means of infection. In addition to the dog and cat, particularly on farms, one must also consider sheep, rabbits, guinea pigs, voles, and possibly squirrels. The evidence is now very good that pigeons are also carriers of Toxoplasma. Dr. H. A. Feldman, working in my laboratory in 1947, recovered Toxoplasma from a pigeon trapped in Cincinnati and showed for the first time the existence of natural infection in these birds in the United States. I should say that except for pigeons we have no adequate evidence at this time that any other birds are carriers of this organism.

So much for the source of the infection in nature.

Diagnosis

What can we say about what may be regarded at the present time as solid evidence relative to the pathogenic effects of Toxoplasma in human beings? Personally, I find it helpful to carry the following classification in mind.

First of all, I think separately of the pathogenic effects resulting from prenatal infection, namely, congenital toxoplasmosis. Secondly, and in a separate category, must be considered the type of pathologic effects that may be produced in human beings when

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the infection is acquired at any time after birth. The evidence is very good that when a pregnant woman becomes infected with Toxoplasma she exhibits either no clinical signs of infection or at least nothing that is clinically characteristic, while in the fetus and especially in the developing nervous system, of which the eye is only one part, the Toxoplasma, as a rule, produce especially severe lesions. There is unquestionably a tremendous difference in the susceptibility of the fully developed or postnatal central nervous system and the embryonic nervous system as regards the pathogenic effects of Toxoplasma.

The effects of toxoplasmic infection *in utero* are now well founded on a number of careful post-mortem studies. However, as regards the question of what happens when the Toxoplasma infect human beings after birth, the information is relatively meager.

The best evidence that human beings can be infected with Toxoplasma without exhibiting any clinically recognizable manifestations is to be found among the mothers who give birth to children with proved congenital infections. However, a certain proportion of human beings—and we do not know what that proportion is at the present time—can develop clinical manifestations as a result of postnatal toxoplasmic infection.

One of the manifestations which has definitely been proved—and I want to separate again the hypothetical from the proved—is encephalitis in children, which, although fatal in the one proved case, is not characterized by destruction of the nervous tissues, such as has been demonstrated in the congenital form. Another type found in adults has been a systemic infection, simulating some of the rickettsial diseases, with rash and pneumonitis. Here, also, the lesions in the central nervous system were minimal. To the best of my knowledge, there is as yet no pathologic evidence that ocular lesions occur as a result of postnatal toxoplasmic infection in man.

You all know that in the last six years the impression has spread that Toxoplasma may be the cause of chorioretinitis acquired after birth as well as prenatally. This diagnosis has been considered in individuals exhibiting chorioretinitis of unknown etiology who also had antibodies against Toxoplasma. The presence of the antibodies has been regarded as presumptive evidence that the chorioretinitis was of toxoplasmic etiology. I should like to point out that that impression developed at a time when the serologic diagnostic tests for toxoplasmosis were as yet poorly developed and their significance not properly evaluated. It is only in the past 18 months that new and quantitative methods have been developed which make the serologic diagnosis of toxoplasmosis somewhat more certain.

Before describing and analyzing the recent methods and data, I should like to state that, in my opinion, there is at the present time no evidence that chorioretinitis can be a manifestation of Toxoplasma infection occurring at any time after birth of the individual. Furthermore, there is also no evidence that a healed chorioretinitis in an individual with an arrested congenital toxoplasmic infection can light up and become an acute chorioretinitis. I know that all that has been hypothesized, but, in my opinion, there is as yet no evidence that it occurs. I should like to stress that I did not say that acute chorioretinitis *cannot* occur in an adult as a result of toxoplasmic infection: I merely said that there is as yet no adequate evidence for it.

I should like to describe the methods that we now have at our disposal to determine whether this does or does not occur. I will not say anything at this point about absolute diagnosis on the basis of isolation of the organism by inoculation in experimental animals or demonstration of the organism in histologic sections, because the opportunity to establish the diagnosis by these methods presents itself almost exclusively in fatal cases. The problem that faces the ophthalmologist is how the diagnosis can be estab-

lished in a patient who survives—and there is reason to believe that some individuals with the congenital disease may survive with residua which predominantly affect the eyes.

Serologic tests

Up until about a year ago, we had one test with which many of you are familiar, that is, the neutralization test in the rabbit's skin. I hope you will forgive me if I go into the details of what these tests are about, because if some of you people are going to ask for serologic tests you ought to know what has to be done and what is being demonstrated. You should know that one cannot grow Toxoplasma in a simple culture medium the way one can grow ordinary bacteria or certain Protozoa.

Toxoplasma multiply only in living, susceptible tissue; we must, therefore, use animals for all this work. In the rabbit neutralization test, we determine the capacity of human serum to inhibit or modify the skin lesions produced by Toxoplasma in the rabbit's skin. A diagram of such a test is shown in Figure 1. The skin of a rabbit's back, from which the hair is clipped, is divided into a number of areas as indicated in the diagram. Toxoplasma, in different dilutions of infected mouse-brain suspension, are inoculated intracutaneously. Skin lesions, diminishing in size with increasing dilution, developed in four to seven days. When these varying dilutions of Toxoplasma-containing tissue suspension are mixed with human serums, some fail to modify the skin lesions,

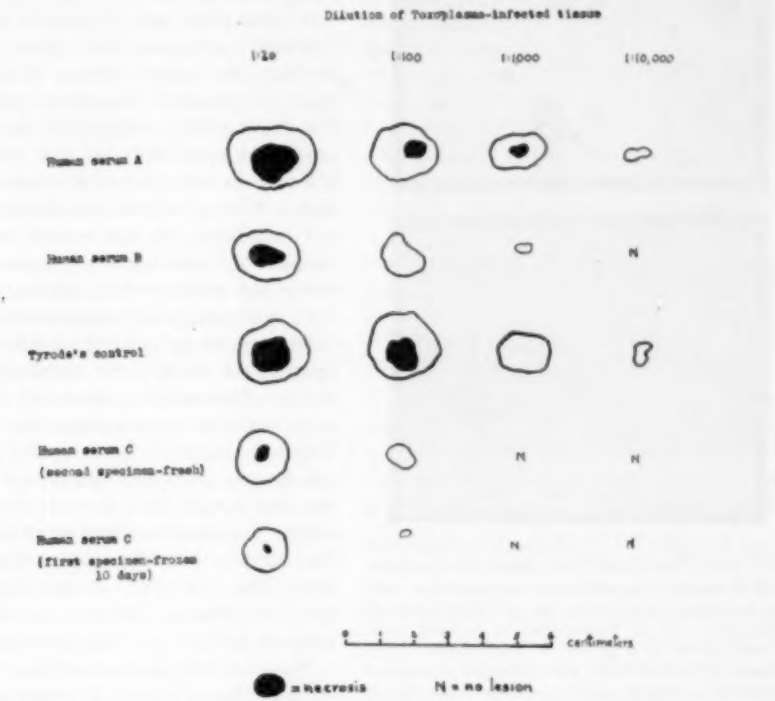

Fig. 1 (Sabin). Tracing of Toxoplasma neutralization test on back of rabbit, seven days after inoculation. (From Sabin, A. B.: Toxoplasmosis: recently recognized disease of human beings, Advances in Pediatrics, 1:1-56, 1942 [Interscience Publishers, New York].)

and these are said to be without antibody. Serums which modify the skin lesions only slightly have been regarded as yielding equivocal results of uncertain significance. The serums which completely inhibit some of the lesions and modify the size of the others have been regarded as being positive for toxoplasmic antibody.

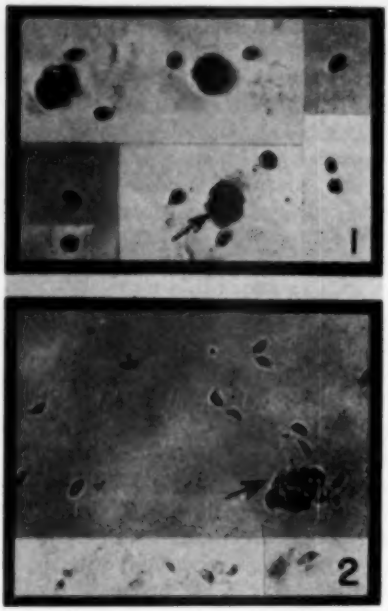

Fig. 2 (Sabin). (1) Toxoplasma incubated with fresh normal serum and then mixed with methylene blue. Note that the organisms are rounded or oval, the cytoplasm stains dark, and the lighter-staining chromatin body is surrounded by a light zone. Arrow points to a group of intracellular Toxoplasma. Different fields are presented because of difficulty of getting organisms into focus in wet preparation. (×650.) (2) Toxoplasma incubated with fresh immune serum and then mixed with methylene blue. Note that the organisms are mostly crescentic, the cytoplasm is unstained except in the intracellular group (arrow), and the chromatin remains stained. Wet preparation. (×650.) (From Sabin and Feldman,[8] p. 661.)

However, there was something very peculiar about the antibody in human serum which produced these effects against Toxoplasma in rabbits. If you sent such a specimen of serum in the ordinary mail, the antitoxoplasmic effect disappeared. If you left it at room temperature for a little while, the antibody effect disappeared and you could not revive it simply by adding some complement in the form of guinea-pig serum. So, you will recall, it was always necessary to send serums for such tests in the frozen state, in dry ice.

Another thing that was peculiar about this "antibody" effect was that, when one tried to dilute the serums even a little bit, this effect disappeared. We, therefore, thought that the antibody was readily destroyed at ordinary temperatures and that it was present only in very low concentration. Many human beings, without any history relative to Toxoplasma, yielded serums which had the same antitoxoplasmic properties, qualitatively and quantitatively, as, let us say, a child with congenital toxoplasmosis or its mother. So we had no way of differentiating between the toxoplasmic "antibody" in the serums of normal individuals and that found in the serum of a mother or a child who were definitely proved to be infected. We could not do very much with this type of antibody test, and it made no difference whether such serum-Toxoplasma mixtures were tested in the rabbit's skin, the chick embryo, or in mice. This type of test yielded only qualitative information. That was the main difficulty up until a very short time ago.

Now I should like to show you a new type of test (fig. 2) which has been elaborated during the past 18 months. It depends on the discovery of an entirely new immunologic principle which has given us an opportunity to study the serologic reactions in this disease in a quantitative manner. In the upper part of the picture you see what happens when Toxoplasma, obtained from the peritoneal exudate of a mouse, are incubated with fresh, normal, human serum which contains *no* toxoplasmic antibody, and some alkaline methylene blue is added to it. Note the staining of the cytoplasm and the chromatin of the extracellular Toxoplasma, as

well as of those inside the leukocytes.

However, when the Toxoplasma were mixed with the fresh serum of a mother who had given birth to a child with congenital toxoplasmosis (or the child's serum in which toxoplasmic antibodies were present), incubated in the same way for an hour and then tested with alkaline methylene blue as the indicator, we found that something very peculiar had happened to the cytoplasm. The cytoplasm of the Toxoplasma had now lost its affinity for the dye. The chromatin still stained the same way. However, that applied only to the organisms which were outside of cells; the intracellular organisms were protected from the action of the antibody and did not show this reaction. We found that the antibody which was responsible for this phenomenon was the same as the neutralizing antibody which we were testing before in rabbits, mice, or chick embryos.

However, the utilization of this phenomenon as the basis of a new quantitative, in vitro test for toxoplasmic antibody depended on still another discovery. That discovery was that the specific antibody was relatively heat stable; that is, it was not destroyed by heating at 56°C. for 30 minutes or by being in the mails at summer temperatures for many days, but that by itself it could neither neutralize the pathogenic effects of Toxoplasma nor modify the affinity of the cytoplasm for certain dyes. To achieve this another substance was necessary.

That substance was very unstable at ordinary temperatures and was present in all human serums in such small amounts that even slight dilution, usually beyond 1:2, was sufficient to reduce it below the effective level. Thus, it became evident that the complete immune phenomenon depended on a heat-stable specific antibody plus a nonspecific, heat-labile factor related to but not identical with the ordinary complement. It also became apparent that what was present in small amounts was the nonspecific accessory factor and that the specific antibody could be present in small or large amounts depending upon the history of the individual's experience with Toxoplasma.[3]

Now let me tell you how this was then used as the basis of the new, quantitative test, which is being called the "dye test" for toxoplasmic antibody. The serum from a suspected case, which can now be shipped without refrigeration, is used to prepare a number of dilutions in saline. To each of these dilutions is added a suspension of Toxoplasma (from the peritoneal exudate of a mouse) in fresh, undiluted, normal human serum which is free of toxoplasmic antibody but contains the important accessory factor. The normal human serum which is the source of the accessory factor can be stored frozen in dry ice and used when needed.

After incubation of these mixtures in a water bath at 37°C. for one hour, small drops from each tube are mixed with the alkaline methylene blue, and the percentage of extracellular Toxoplasma whose cytoplasm remains unstained is determined.

The dye test titer refers to the highest original dilution of a serum which, in the presence of a constant, adequate amount of accessory factor, is capable of depriving the cytoplasm of 50 percent of the Toxoplasma of its affinity for methylene blue at pH 11.0.

By this method it was possible to show that experimental animals and human beings with proved recent toxoplasmic infections yielded serums with dye test titers in the range of 1:1,000 to 1:16,000. Such serums in the old rabbit test could not be differentiated from "normal" human serums with toxoplasmic antibodies; however, the dye test titers of such "normal" human serums have rarely exceeded 1:64.

During this same period, an improved, quantitatively controlled complement fixation test has been developed utilizing ultracentrifuged extracts of Toxoplasma-infected chorioallantoic membranes of embryonated eggs as the antigen.[5] In experimental animals, we have found that the dye test antibody appears in three to five days after inoculation with Toxoplasma and reaches peak

titers of 1:1,000 to 1:4,000 in 10 to 21 days, while the complement-fixing antibody appears later and can still be absent three to four weeks after infection. However, both of these antibodies have been found to persist in high titer for many months and years

children who exhibited chorioretinopathy associated with various other manifestations of cerebral damage. The question in all of these was whether the diagnosis was toxoplasmosis. The results[9] have recently been published.

TABLE 1

QUANTITATIVE TOXOPLASMA ANTIBODY TESTS ON CHILDREN EXHIBITING CHORIORETINOPATHY WITH OTHER SIGNS OF CEREBRAL DAMAGE AND ON THEIR MOTHERS

Group	Time (months after birth)	Children			Mothers		
		No.	Dye Test Titers	Complement Fixing Titers	No.	Dye Test Titers	Complement Fixing Titers
Serologically compatible with congenital toxoplasmosis	0–5	4	4096, 1024 1024	0, 32, 32, 128	5	1024, 1024 4096, 1024 2048	32, 64, 32 32, (16), 32
	6–23	6	4096, 1024 1024, 1024 4096, 16384	32, 16, 2 32, 32, 128	6	1024, 4096 1024, 1024 1024, 256	16, 32, 4 16, 32, 4
	24–71	6	256, 1024 128, 1024 1024	64, 64, 128 8, 16, 16	6	256, 256 256, 256 32, 1024	64, 16, 64 8, 4, 16
	72–84	4	64, 64 16, 16	8, 16, 0, 2	2	128, 64	8, 32
Serologically *not* congenital toxoplasmosis	0–5	5	0,0,0,0,0	0,0,0,0	5	4,0,0,0,0	0,0,0
	6–23	14	Undil.0,0,0,0,0 0,0,0,0,0,0,0,0	0,0,0,0,0,0 0,0,0,0,0,0	14	4,4,4,16,16, <64 64,0,0,0,0,0,0,0	8,2,2,0,0,0 0,0,0,0,0,0
	67	1	0	0	1	0	0

(From Sabin and Feldman,[9] p. 298.)

and it is, unfortunately, not possible to say that a high titer of either antibody is indicative of an active or persistent infection. The dissociation between the two types of antibody during the early stage of toxoplasmic infection may, perhaps, provide the only serologic means by which activity may be detected. Thus, if a serum had a high titer of dye test antibody (1:256 or more) with little or no complement-fixing antibody, the latter, however, increasing in titer subsequently, there would be a reasonable basis for suspecting an active infection during that particular interval of time.

Now I should like to discuss with you the results we obtained with the aid of these new diagnostic methods in a group of 43

It is evident from the results shown in Table 1 that these children fell into two distinct groups—one serologically compatible with a diagnosis of *congenital* toxoplasmosis (because, in all instances, their mothers' serums also yielded the high antibody titers found in association with proved toxoplasmic infection), and the other without serologic evidence of toxoplasmosis. In the serologically positive children, aged up to 23 months, the dye test titers were all in the range of 1:1,024 to 1:16,384, and all but two of the 10 children in this group had complement-fixing antibody titers of 1:16 to 1:128.

The one child, aged five weeks, whose serum gave a completely negative test for the complement-fixing antibody, nevertheless

had a dye test titer of 1:4,096. You will recall my earlier remark that such dissociation of the two antibodies was found during the early stages of active infection in experimental animals, and it is important to note that this particular child died several days later with signs of active encephalomyelitis. The other child, with a complement-fixing titer of 1:2 and dye test titer of 1:1,024 at the age of 15 months, showed the same results in a specimen of serum taken at 30 months of age. This suggests to me that the complement-fixing antibody either may be very low in some patients or may disappear rather rapidly, and that, therefore, it is not advisable to rely on this test alone. The dye test and complement fixation test together give us more information than either one of them alone.

The results from the children over two years of age and from their mothers in the serologically positive group indicate that, while the toxoplasmic antibody titers can remain high for a number of years, there is a definite tendency for them to drop as the years go by. For this reason, after six to seven years it may be difficult to establish the diagnosis of congenital toxoplasmosis with certainty in the individual case. The data on the mothers in this group also provided us with evidence that high dye test and complement-fixing toxoplasmic antibody titers do not necessarily indicate persistent infection. Seven of the mothers with these high antibody titers gave birth subsequently to children who were normal and free of any evidence of congenital toxoplasmic infection. One can say that in these mothers the toxoplasmic infection was either completely "burned out" or under sufficient control to prevent transmission to subsequent children.

In the serologically negative group of children, it is noteworthy that among the mothers' serums 40 percent gave positive tests for toxoplasmic antibody by the dye test and 15 percent by the complement-fixation test. Notice, however, how low the titers are in this group by comparison with those found in the mothers whose children were also serologically positive. Actually, the mothers of the serologically negative children exhibit about what has been found in the population at large in the same age group.

In former years, when one found a child with chorioretinopathy and certain other signs that might suggest congenital toxoplasmosis associated, however, with negative or equivocal tests for toxoplasmic antibody in the child's serum and positive results in the mother's serum—by the rabbit method—there was a tendency to interpret these as instances of congenital toxoplasmosis in which the child had failed to develop antibodies (and there are many such case reports in the pediatric and ophthalmic literature). The serologic pattern obtained by the new quantitative methods is such that now there appears to be no justification for considering the diagnosis of toxoplasmosis in the absence of conclusive serologic data.

The assumption, previously entertained, that the toxoplasmic antibodies may disappear quickly in some individuals or that infants may be slow in developing their own upon losing the placentally transmitted maternal antibody is now without valid evidence and, therefore, untenable.

Our studies[4] on placental transmission of toxoplasmic antibody indicate that when the child is not infected the antibody has either entirely disappeared or dropped to a negligible titer by the end of four months. This must be borne in mind in establishing the diagnosis in doubtful cases.

The most important conclusion from this study of 43 children is that there exists a syndrome, most probably congenital and of which chorioretinopathy is one manifestation, which clinically simulates healed congenital toxoplasmosis but which is not due to toxoplasmic infection. I can tell you that the 20 patients in the nontoxoplasmic group were accumulated in a much shorter time than the others, and it is my impression that this syndrome probably is more fre-

quent than congenital toxoplasmosis.

A very interesting correlation with reference to the incidence of cerebral calcification appeared when we analyzed the other clinical manifestations of these two groups of children with chorioretinopathy (table 2). Among the 23 children with positive serologic evidence of toxoplasmosis, 87 percent had cerebral calcification associated with the chorioretinopathy, while among the 20 children with negative tests for toxoplasmic antibody, only five percent had cerebral calcification. I must say that in a few of the X-ray films of the skull we had to look pretty hard to find the minute foci of calcification, but we looked just as hard in both groups. Thus, it may be possible to formulate the following useful clinical guide for the ophthalmologist. If the chorioretinopathy of presumable congenital origin is associated with cerebral calcification, the chances are approximately 9 to 1 that serologic tests will prove it to be due to congenital toxoplasmosis; on the other hand, if it is not associated with cerebral calcification, the chances are approximately 9 to 1 that it is *not* due to toxoplasmosis.

TABLE 2

INCIDENCE OF CEREBRAL CALCIFICATION AMONG CHILDREN EXHIBITING CHORIORETINOPATHY AND OTHER EVIDENCE OF CEREBRAL DAMAGE IN RELATION TO SEROLOGIC EVIDENCE OF CONGENITAL TOXOPLASMOSIS

Serologic Evidence of Congenital Toxoplasmosis	Age Group (years)	No.	Cerebral Calcification Percentage Positive
Positive	Under 2	13	92
	2–7	10	80
	Total	23	87
Negative	Under 2	19	5
	2–7	1	0
	Total	20	5

(From Sabin and Feldman,[2] p. 299.)

I want to stress, however, that in the individual case the diagnosis must still be made by the serologic tests. It is important to do this not only for academic reasons but also because it permits the physician to tell the parents that the outlook for a subsequent normal child is good when the diagnosis of congenital toxoplasmosis can be confirmed. In the nontoxoplasmic group, where chorioretinopathy is associated with other evidence of cerebral damage, we still do not know enough about familial and other underlying factors to be able to say anything.

PATHOLOGIC MANIFESTATIONS

Now I should like to show you certain pathologic manifestations which have been encountered post mortem in patients with nontoxoplasmic congenital chorioretinopathy. For comparison, however, I should first like to show the eyes of a child with congenital toxoplasmosis who died at eight and one-half years of age. I observed this child from the time it was about six months of age when the diagnosis was first established by serologic methods. Note (fig. 3) the "punched-out" lesions in the macular region and elsewhere in the retina of one eye, and the single lesion in the retina of the other eye. Histologic examination of these lesions revealed only scar tissue and very scanty infiltration with mononuclear cells. No Toxoplasma were found anywhere in the eyes or brain, which showed extensive destruction with hydrocephalus and bone formation in the calcified areas. However, even at six months of age, brain tissue obtained by cortical biopsy revealed no Toxoplasma by histologic examination or animal

inoculation. This may be taken as an example of a congenital toxoplasmic infection which was "burned-out" very early in life.

It is my present impression that in the group of children with chorioretinopathy and other evidence of cerebral damage but without cerebral calcification and not associated with toxoplasmic infection, we are dealing with lesions which most likely represent defective development rather than healed, inflammatory foci. The first patient belonging to this group that we have had an opportunity to study post mortem (at one year of age) fits this hypothesis very well. In Figure 4, you see the eyes of this patient —one with microphthalmus and microcornea and the other normal in size. During life, funduscopic examination of the microphthalmic eye was impossible, while in the other eye a lesion was found in the macular area which was described as an "old, healed chorioretinitis." On section (fig. 5), the microphthalmic eye showed a retrolental mass, extending from the lens to the disc, apparently enveloped by the detached retina.

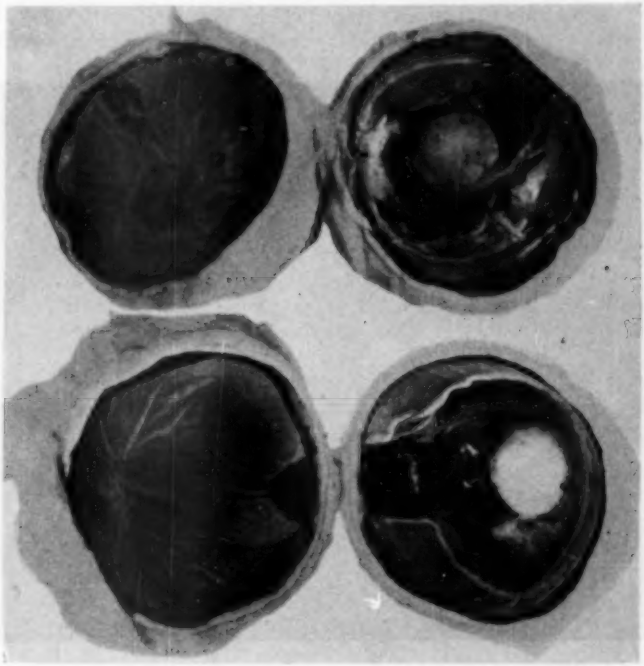

Fig. 3 (Salán). Eyes of a child (R. B.) with congenital toxoplasmosis, dead at eight and one-half years of age. Photographed after fixation in Verhoeff's solution (formalin, alcohol, and picric acid).

Microscopically the mass consisted of fibrovascular tissue with retinal elements scattered irregularly through it. Of particular interest was the fact that the retinal tissue and pigment were found for a considerable distance within the optic nerve. In the other eye, one can see grossly the lesions in the macular area and elsewhere in the retina, which were apparent on ophthalmoscopic examination. Microscopically, this eye showed evidence of defective development rather

than scarring with inflammatory reaction; in some areas the normal retinal tissue was missing with pigment showing through and in others very little pigment was present. In this eye, also, extensive retinal rests were found within the optic nerve. Defective development was also evident in the brain of this child—it was smaller than normal, there were many microgyri, the posterior horns of the lateral ventricles were open, and many cysts were found in the choroid plexus. There was no evidence of any inflammatory or destructive process and no calcification.

In addition to this noninflammatory, defective development type of syndrome, I have recently come across another condition in infants characterized by chorioretinopathy, hydrocephalus with extensive destruction of brain tissue, cerebral calcification, and psychomotor disturbances, *but* unassociated with any evidence of toxoplasmic or other infection. The first instance of this condition I studied through the courtesy and coöperation of Dr. Gilbert J. Levy and Dr. W. W. Tribby of Memphis, Tennessee.

The eye lesions, which during life were described as "healed chorioretinitis," presented neither destructive nor inflammatory changes and consisted of retinal and choroid atrophy. The brain, however, presented extensive destructive, noninflammatory lesions associated with extensive calcification and, in the softened areas, peculiar degenerative changes in many of the small blood vessels.

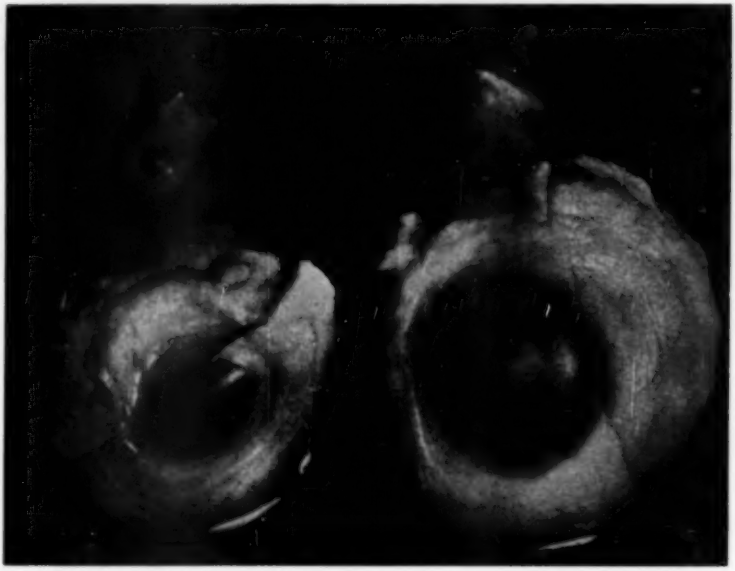

Fig. 4 (Sabin). Eyes of child (L. O.) with nontoxoplasmic chorioretinopathy and associated cerebral damage—dead at one year of age.

These vascular lesions consisted of an eccentric thickening of the walls filled with hyaline or amorphous, granular or fibrillar, acidophilic material staining a deep purple with phosphotungstic acid hematoxylin.

Shortly thereafter, through the courtesy of Dr. R. V. Platou and Dr. John Dent of New Orleans, I saw postmortem material with similar vascular lesions in an infant who also exhibited chorioretinopathy, cerebral calcification, and hydrocephalus, but without lesions suggestive of toxoplasmic or other infection.

So much for the differential diagnosis of

chorioretinopathy which is seen in early childhood, which may be assumed to be of congenital origin. The main thing to remember is that some are caused by Toxoplasma and others not, and the only way to be certain in the individual patient is by use of the quantitative methods recently described. When "healed" chorioretinopathy is first discovered in school-age children, the possibility of its being a healed, congenital toxoplasmic lesion can be entertained when the serums of both the mother and the child contain toxoplasmic antibodies, even of low titer, because the incidence of such antibodies in normal children under 15 years of age is probably less than 10 percent. It should be realized, however, that in the individual case such positive serologic evidence constitutes high probability but not proof that the eye lesion is due to toxoplasmosis. Since after 15 years of age the incidence of toxoplasmic antibodies in the normal population begins to rise very abruptly, it becomes increasingly more difficult to correlate chorioretinitis of unknown etiology in adults with mere presence of such antibodies.

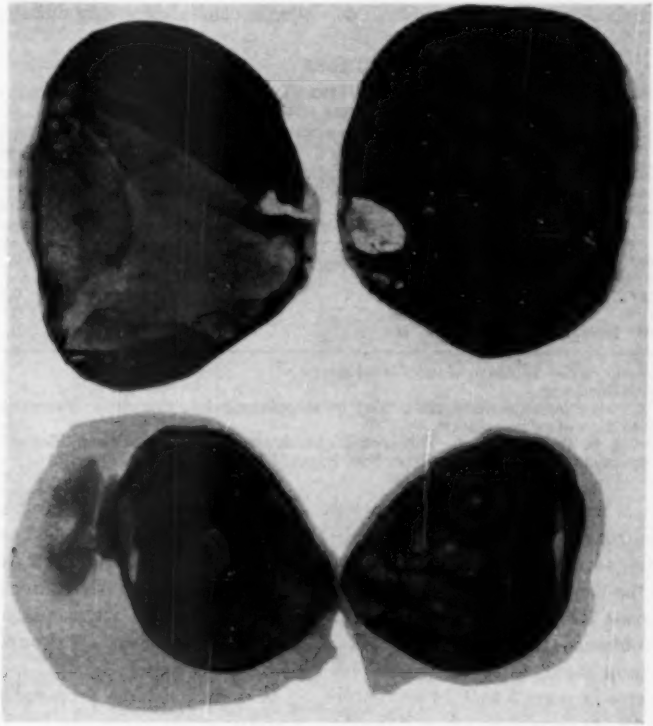

Fig. 5 (Sabin). Same as Figure 4. Photographed after fixation in formalin.

Significance of skin test

Since it has been maintained in several recent publications that the incidence of positive skin reactions to Toxoplasma antigen is very much higher in adults with chorioretinitis of unknown etiology than in others, and since this has been offered as evidence of the toxoplasmic etiology of the chorioretinitis, I should like to discuss the present status

of the significance of this skin test in patients.

The skin test with Toxoplasma antigen (called toxoplasmin by Frenkel) in human beings is considered positive when a delayed tuberculin-type reaction appears. Dr. H. A. Feldman and I[3] have used extracts of Toxoplasma-infected chorioallantoic membranes, and of normal membranes of embryonated eggs for control, to study the reactions obtained in the "normal" population of different ages in the Cincinnati area.

With at least 20 individuals in each age group, we obtained the following results: none positive in the 0- to 4-year group, five percent positive in years 5 to 9, 14 percent in years 10 to 19, 20 percent in years 20 to 29, 50 percent in years 30 to 39, 65 percent in years 40 to 49, and 65 percent in years 50 to 81.

But what does a positive or negative skin test mean as an indicator of toxoplasmic antibody? We found that all people who gave a positive skin test also had antibody in their serum by the new dye test. However, those who had a titer of 1:4 gave just as strong a skin reaction as those with a serum titer of 1:4,000. Furthermore, the reverse did not obtain: a considerable proportion of normal people, and also some with proved toxoplasmic infection, who gave negative skin tests had antibody of varying titer in their serum.

I regard the skin test as being of no value for diagnostic purposes because a negative test does not indicate absence of antibody or infection, and a positive skin test does not differentiate between individuals having a titer of such dubious significance as 1:4 and those with the highly significant titers of 1:256 or more. The skin test may, nevertheless, be used as a crude tool for population surveys and group correlation studies, provided such studies are properly controlled as to "normal" antigen, age grouping, and place of birth or residence.

Why such a large proportion of the adult population has antibodies for Toxoplasma is not at the present time altogether clear. Undoubtedly in some instances this is due to inapparent or unrecognized infection with Toxoplasma, but we cannot as yet be certain that in other instances, particularly in the very low titer group, this may not be due to infection with an as yet unknown agent possessing a common antigen with Toxoplasma. For this reason, I believe that not until it can be shown that acute uveitis and chorioretinitis of the noncongenital variety are associated with the high titers of antibody found in proved instances of inapparent or clinically recognized toxoplasmic infection

TABLE 3

EFFECT OF SULFATHIAZOLE IN DIET ON TOXOPLASMIC INFECTION BY INTRACEREBRAL ROUTE IN MICE

Dilution of Toxoplasma-Infected Brain Suspension	Controls No Drug in Diet	1% Sulfathiazole in Diet for 21 Days After Intracerebral Injection of Toxoplasma	
		Mice Dying While on Drug	Mice Dying After Removing Drug
10^{-1}	4, 5, 5*	0, 0, 0	0, 0, *33*
10^{-2}	6, 6, 6	0, 0, 0	*36*, *47*, *51*
10^{-3}	6, 6, 7	0, 0, 0	0, *54*, *54*
10^{-4}	7, 7, 7	0, 0, 0	0, 0, *46*
10^{-5}	8, 9, 0	0, 0, 0	0, 0, 0

* Numerals refer to day of death of inoculated mouse.
0—Mouse remained well.
Numerals in italics indicate mice which died to toxoplasmic infection after discontinuance of drug; numbers refer to days after inoculation.
(From Sabin, A. B. and Warren, J.: Therapeutic effectiveness of certain sulfonamides on infection by an intracellular protozoon (Toxoplasma). Proc. Soc. Exper. Biol. & Med., 51:22, 1942.)

will it be possible to assign an etiologic role to this parasite in this condition. The few patients in this category whom I have had an opportunity to study thus far yielded only the low titers found in the normal population at a time when the ophthalmologist considered the ocular condition as relatively acute. If a patient with acute chorioretinitis exhibited shortly after onset a dye test titer of 1:256 or more and a negative result or low titer in the complement fixation test which, however, rose very appreciably several weeks later, there would be valid serologic evidence for considering a toxoplasmic etiology in such a case, But, let me add, this has not as yet been demonstrated.

TABLE 4

EFFECT OF DELAYING SULFATHIAZOLE THERAPY ON TOXOPLASMIC INFECTION IN MICE

Time after Infection 1% Sulfathiazole Diet Begun	Total Time on Diet, (days)	No. of Mice	% of Mice Surviving One Month	% of Mice Cured	Day of Death of Succumbing Mice
Immediately	23	9	100	78	*37, 37*
2 days	28	9	67	56	8, 14, *20, 42*
4 days	26	19	47	0	8, 8, 8, 9, 11 12, 13, 13, 13, 21 *40, 40, 40, 42 42, 42, 42, 42, 44*
5 days	Duration of experiment	10	0	0	6, 6, 6, 8, 8 8, 8, 11, 11, 15
6 days	"	10	0	0	7, 7, 8, 8, 8 8, 8, 8, 8, 8
6 days 2 mg. t.i.d. by stomach tube on 6th day + diet	"	10	10	0	7, 7, 7, 7, 7 7, 8, 8, 8, *46**
Untreated controls	—	20	0	0	7, 7, 7, 7, 8 8, 8, 8, 8, 8 8, 8, 8, 8, 8 8, 9, 9, 9, 10

Legends as in table 3.

* This mouse was on the sulfathiazole diet for 22 days.

All mice were inoculated intra-abdominally with 0.3 cc. of a 1:100 suspension of Toxoplasma-infected brain —about 100 M.L.D.

(From Sabin, A. B. and Warren J.: Therapeutic effectiveness of certain sulfonamides on infection by an intracellular protozoon (Toxoplasma), Proc. Soc. Exper. Biol. & Med. 51:21, 1942.)

THERAPY

I was also requested to say something about specific therapy. Although various drugs have been found capable of killing Toxoplasma in vitro, they were without effect in vivo. The sulfonamides, which are without effect on Toxoplasma in vitro, are the only ones thus far shown to exert a distinct therapeutic effect in experimental animals. A typical experiment in mice is presented in Table 3. This shows that one percent sulfathiazole in the diet completely held the infection in check, even when 10,000 minimal lethal doses were inoculated directly in the brain, for as long as the drug was being consumed and for a considerable time thereafter. It should be noted, however, that about 50 percent of the mice ultimately died of toxoplasmosis when the drug was discontinued.

Another type of experiment, in which the effect of delaying sulfathiazole therapy in mice is studied (table 4), indicates that with a dose of Toxoplasma which kills all untreated animals in 7 to 10 days, a delay of

two days reduces the percentage cured from 78 to 56, and a delay of four days reduces the ultimate effectiveness of the drug to zero. It is noteworthy that it is easier to cure rabbits than mice, apparently because treated rabbits develop immunity while the mice do not.*

Is there any point at all in administering sulfonamides to an infant with congenital toxoplasmosis? I see none. The lesion and the damage that has been done are, as a rule, already so far advanced that I do not think anything whatever can be gained. Is there any point in administering sulfonamides to an individual with an acute chorioretinitis which may possible be due to toxoplasmosis? I would say that when the day comes when such a diagnosis can be entertained with assurance—then, yes; but that day has not yet come, and the existence of noncongenital, acute toxoplasmic chorioretinitis still has to be demonstrated.

Let me consider still another possibility which applies not to ophthalmologists but to obstetricians. Some obstetricians have begun to study women in the prenatal clinic to see whether or not they can pick up an acute toxoplasmic infection during the course of the pregnancy. I would say that if an obstetrician finds a woman who has a very high titer of dye-test antibody and has no complement-fixing antibody, there is a good possibility that she is undergoing an acute infection with this organism and, in such a case, I think, yes, there is an indication for giving sulfonamides in the hope of preventing a congenital toxoplasmosis.

I understand that some ophthalmologists, on the suggestion of Dr. Frenkel, have been administering Toxoplasma antigen to patients exhibiting acute chorioretinitis or a hypothetic acute exacerbation of a chronic retinitis. In my opinion, there is at present no adequate evidence that there is such a thing as an acute exacerbation of a congenital toxoplasmic chorioretinitis and, as was pointed out before, no evidence that noncongenital acute chorioretinitis is caused by Toxoplasma. Furthermore, even if there were, I cannot see what the administration of small amounts of Toxoplasma antigen can possibly do to such a lesion.

I have one message that I should like to leave with my ophthalmic colleagues and that is—make a study with the new serologic methods of those cases of acute chorioretinitis in children and adults which are of unknown etiology to determine whether or not and to what extent toxoplasmosis may be involved. For the present, however, the ophthalmologist has good reason to consider toxoplasmosis only in the differential diagnosis of chorioretinopathy of congenital origin.

Elland and Bethesda Avenues (29).

* Since this paper was presented, Summers reported that aureomycin also is an effective therapeutic agent against Toxoplasma in mice. (Summers, W. A.: The effects of oral administration of aureomycin, sulfathiazole, sulfamerazine and 4,4'-diamino diphenyl sulfone on toxoplasmosis in mice. Am. J. Trop. Med., **29**:889-893 [Nov.] 1949.)

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PLASTIC SOCKET AND LID RECONSTRUCTION*

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The purpose of this report is to present a series of procedures used in the construction of an eye socket and lids and to point out the advantages of close coöperation between the ophthalmologist, the plastic surgeon, and the prosthesis technician. The procedures are not new, although each plastic operation should be individually designed within the framework of surgical principles and procedures as applied to plastic surgery.

CASE REPORT

History. The patient (No. 14759), a 21-year-old white veteran, was hit in the right eye, on November 8, 1947, by a piece of hot metal which penetrated the globe and inflicted third-degree burns of the lids which subsequently sloughed. Fifteen hours later he was admitted to the Veterans Administration Hospital at Huntington, West Virginia, where he was treated conservatively until the reaction had subsided. On December 1, 1947, an enucleation of the remains of the globe was done and a 14-mm. glass ball was buried in the salvaged portion of Tenon's capsule and covered by suturing the rectus muscles over the ball. Since there was no remaining conjunctiva, the stumps of the lids were brought together.

Examination. On December 15, 1948, the patient was transferred to the Fort Howard Veterans Administration Hospital for plastic reconstruction. At this time his general history, system review, physical examination, serology, chest X-ray studies, urinalysis, and blood studies were entirely unremarkable. The site of injury was covered by healthy skin which was under a moderate degree of tension, and the horizontal scar from the fusion of the lid stumps was well healed.

Fig. 1 (Scarborough and Landers). The patient as he appeared on admission in January, 1948. The scar of the approximation of the lid stumps under tension can be seen.

There was nothing to suggest the presence of tarsi or of levator action.

Operation. On December 27, 1948, under sodium-pentothal anesthesia, the horizontal scar resulting from the closure of the lid stumps was excised, and the skin was undermined above and below from 10 to 15 mm. (plate 1, fig. 1). This immediately retracted leaving an oval denuded area 65 by 64 mm. in size.

A gauze pattern was cut and a full-thickness graft, including only epidermis and dermis, and of the same size, was taken from the supraclavicular triangle of the left side of the neck. This was secured in place with single 5-0 black-silk sutures, the ends of which were left very long (plate 1, fig. 2). One layer of gauze, lightly impregnated with

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* The Veterans Administration assumes no responsibility for the opinions expressed or the conclusions drawn by the authors.

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boric acid ointment, was cut to size and placed exactly over the graft. This was followed by a thick pad of sterile mechanic's waste, over which the long ends of the silk skin sutures were tied in groups of three strands. More mechanic's waste was packed around the area and a snug pressure bandage was applied.

The first dressing was done after five days at which time the "take" of the graft was complete except for a four-mm. slough directly over the buried glass ball. There was a somewhat redundant roll of skin at the superior margin due to undermining of the skin edges in order to get in as much skin as possible to allow for shrinkage of the graft.

Socket reconstruction. After complete healing and a period of rest at home, the reconstruction of a socket was undertaken on April 22, 1948. A horizontal incision was made in the graft to correspond to the opposite lid fissure (plate 1, fig. 3). This was two mm. higher than the lid fissure on the opposite side to allow for sagging, and at each end the incision was brought to a minute Y shape in order to construct canthi.

The five-mm. healed area of slough was excised in the line of incision which was then carried backward on a bevel of approximately 40 degrees to the orbital rim, except on the nasal aspect, at a point corresponding to the opposite inner canthus where undermining is not desirable (plate 1, fig. 4). This dissection was deep to the fibers of the orbicularis. Care was exercised to leave an adequate covering of 2 to 3 mm. for the underlying glass ball implant. All bleeding was controlled in the freshly dissected cavity by adrenalin packs.

A 50 by 80 mm. split skin graft approximately 0.3 mm. thick, cut from the right thigh in a hairless area, was placed over the mouth of the cavity, raw surface down (plate 1, fig. 5), and sterile mechanic's waste was packed into the cavity through the lips of the newly constructed fissure in the full-thickness graft in such a manner that the split skin graft completely lined the cavity and was held against its inner surface by the pressure of the mechanic's waste. The graft spread beyond the edges of the incision all the way around, thus making sutures unnecessary. A single layer of vaseline gauze was placed over the entire area, which was then covered by mechanic's waste and a pressure dressing.

On the seventh day, at the first dressing, it was found that the socket was completely epithelized except for the very edge at which there was a fine line where the excess split skin had overlapped the intact skin edges. There, the full-thickness graft and the split

Plate 1 (Scarborough and Landers). (Fig. 1) The superficial dissection in which the horizontal scar from the suturing of the lid stumps was removed, and the surrounding skin was undermined to receive a large skin graft for the following procedures.

(Fig. 2) The full-thickness graft from the neck in place, secured by 5-0 black silk, the ends of which were left very long in order to tie them in groups over sterile mechanic's waste to exert uniform pressure.

(Fig. 3) The approach to the problem of constructing a socket to receive the prosthesis. The incision is indicated. The fully healed graft, in spite of shrinkage, is under no tension as shown by the slightly redundant roll laterally and above.

(Fig. 4) The dissection for the socket, showing the undermining at increasing depth, to insure the blood supply at the socket margins. The area of the inner canthus was left intact for anchorage at this point.

(Fig. 5) The socket lined by split skin graft from the leg, the edges of which widely overlap the margins of the fissure and thus do not require sutures. The cavity was packed to maintain even and complete contact.

(Fig. 6) The construction of an upper lid by dissection of a semicircular flap from the outer full-thickness graft above the socket margin. This flap was turned downward over a pack and sutured to the lower edge of the socket. The dotted line indicates the socket margin.

(Fig. 7) The denuded area, resulting from the dissection shown in Figure 6, covered by a full-thickness graft of thin skin from the neck. The long ends of the sutures were tied over mechanic's waste to maintain perfect approximation.

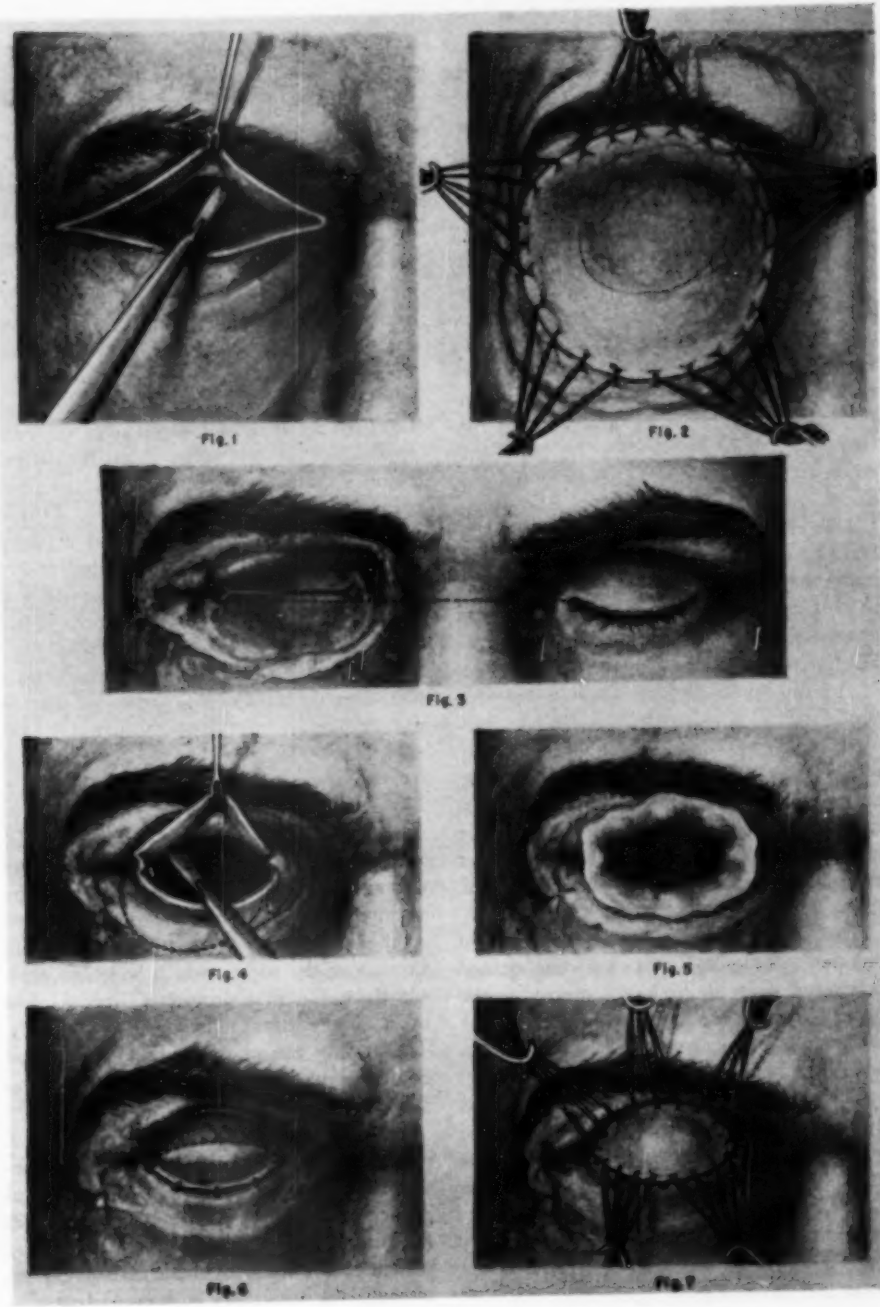

Fig. 1

Fig. 2

Fig. 3

Fig. 4

Fig. 5

Fig. 6

Fig. 7

skin graft had not yet completely united. The socket was relined by a single layer of boric acid gauze and repacked. The edges healed promptly.

Fourteen days following the operation, the patient was sent to the Veterans Administration Prosthesis Laboratory in Baltimore* where a plastic eye was made to fit the space. During the period of healing, and while the prosthesis was being constructed, the newly fashioned socket was kept packed to prevent shrinkage. Since there was no lacrimation and no conjunctiva, there was no difficulty from odor or from skin desquamation such as is found when skin is used alongside normal conjunctiva in lining a socket. The patient was taught to massage the graft with cocoa butter twice daily to soften the skin for the next procedure.

Lid reconstruction. After a period at home, the construction of an upper lid was undertaken on July 2, 1948. The technique of this operation was very simple, but the execution required meticulous care. A semicircular area was marked out on the surface of the full-thickness graft above the eye fissure from the external to the internal canthus. This curved upward a little over 10 mm. from the socket margin. A shallow incision followed this line and a flap was undermined to the edge of the fissure. This began at a thickness of one mm. and became thicker as it progressed so that, at the fissure margin, it was 4 to 5 mm. thick.

The socket was packed with boric-acid ointment gauze and this flap was turned downward over the pack and sutured to the lower border of the fissure, thus creating the inner surface for an upper lid (plate 1, fig. 6).

The denuded area above the fissure and the now continuous denuded outer surface of the flap were covered by a full-thickness graft from the lower right neck by the same technique as the original full-thickness graft (plate 1, fig. 7).

Four days later, the pack was removed from the socket and the prosthesis placed in it. The newly constructed lid, as might be anticipated from the mode of its construction, did not fit well at the canthi. This was particularly true at the inner canthus which was too wide.

On August 24, 1948, an advancement of the inner corner of the new lid was done. A triangular flap composed of the medial portion of the right upper lid was raised and moved medially and downward to fit into a bed previously prepared for it by the removal of a similarly shaped area of skin. This flap was secured by a No. 40, white-cotton subcutaneous suture at the extreme point of advancement (plate 2, fig. 1) and the skin edges were approximated with 5-0 black silk (plate 2, fig. 2). This healed uneventfully, after which the prosthesis was again placed in the socket and cocoa-butter massage instituted to soften the skin.

On October 19, 1948, a similar procedure was done just below the inner canthus to narrow the inner part of the palpebral fissure. This was done by two inverted V incisions, one within, or below, the other. The area between was excised and the lower point advanced to fill the gap (plate 2, fig. 3). Again the No. 40, buried cotton suture was used to secure the advanced point in position and the skin was closed as before. At the same operation most of the redundant skin above the socket, which had been present since the first procedure, was excised by a simple eliptical excision and closure. The healing was uneventful and the desired result of narrowing the inner canthus was achieved.

On December 23, 1948, a modified Z plasty was done at the external canthus because of poor approximation of the lateral border of the lid to the prosthesis (plate 2, figs. 4 and 5). This was successful and the patient was sent home with instructions to massage the area daily with cocoa butter.

* The technical work on the prosthesis was done under the direction of John C. Heck, D.D.S., to whom we wish to express appreciation.

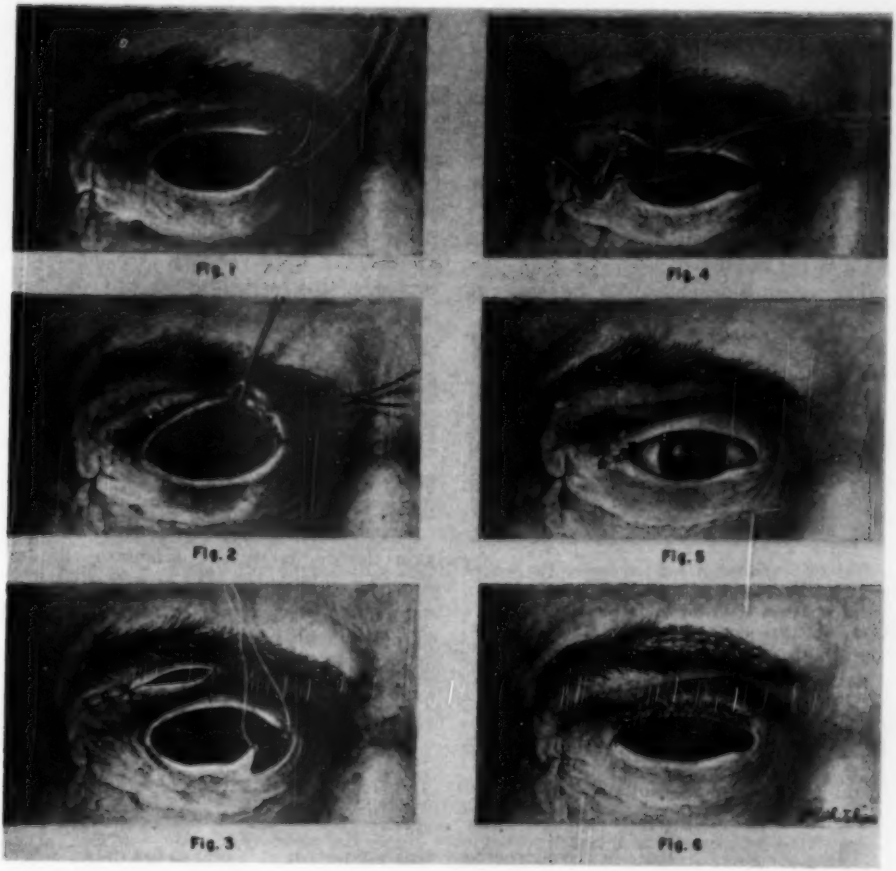

Plate 2 (Scarborough and Landers). (Fig. 1) The first "tailoring" procedure in which the width of the fissure at the inner canthus was reduced by downward advancement of the inner corner of the reconstructed lid. The subcutaneous tension suture is No. 40 white cotton.

(Fig. 2) The completed advancement shown above.

(Fig. 3) Further narrowing of the fissure at the inner canthus by upward advancement of its lower medial border. The excess skin above was removed by simple excision.

(Fig. 4) "Snugging" of the reconstructed external canthus by a modified Z plasty for better fit of the prosthesis. The final positions of the points of the Z are indicated by the tension sutures.

(Fig. 5) The completed reconstruction as described above with the plastic prosthesis in place.

(Fig. 6) The grafting of a narrow strip of skin from the eyebrow to the upper lid to provide eye lashes.

Postoperative course. He returned for observation one month later at which time several attempts were made to furnish eye lashes by implanting stiff black nylon bristles in the prostheses at the upper lid margin, and by fastening a strip of artificial eye lashes to the surface of the plastic eye. These attempts were entirely unsuccessful.

Therefore, on January 27, 1949, a 25-mm. strip of skin approximately 3 to 4 mm. wide and containing hair follicles was taken from the right eyebrow and sutured in a groove

prepared for it just above the upper lid margin (plate 2, fig. 6). This was secured in place by at least 30 minute 5-0 silk sutures and covered by boric-acid gauze and a pressure dressing.

Initially all the hair came out of the graft although there was no slough. However, after a period of two months at least 30 lashes are present. Their direction is not uniform but they can be trained.

The patient is delighted with the results of his many reconstructive operations. He has returned to a useful occupation and has learned to face the world with confidence and assurance.

Fig. 2 (Scarborough and Landers). The patient as he appeared in March, 1949. A little more skin might be taken from the graft above the eye at a later date, depending on further shrinkage.

Discussion

There are several points in reconstructive surgery on which we should like to comment. General anesthesia, preferably intravenous, is almost essential because of the distortion of tissues from local infiltration and the likelihood of the patient becoming restive during the time-consuming procedures.

Skin-graft areas, in fact the plan of the operation, should be diagrammed on the skin with methylene blue on a wood splinter, or by some similar method. In marking out areas to be transferred it is well to allow 20 percent for retraction and the initial area should be made correspondingly large to allow for a similar shrinkage later.

All bleeding must be controlled in an area prepared to receive a graft, and the graft must be kept in intimate contact with the recipient area by a uniformly distributed pressure. Tension on the skin sutures should be avoided, but, if unavoidable, even slight tension should be carried by subcutaneous fine white suture material with the ends cut at the knot.

No. 80 white cotton or 5-0 or 4-0 white silk sutures are ordinarily satisfactory for subcutaneous closure. However, No. 40 white cotton single sutures are preferable, as in the preceding instances where some degree of tension was present. Care must be exercised to avoid tying the fine 5-0 silk sutures of the skin closure too tightly, otherwise the sutures cut through. Just enough pressure to maintain approximation is adequate. There is no rule as to how many skin sutures should be placed in a given area, although very fine sutures every two mm. are not too many.

Vaseline, particularly on fresh graft areas, seems to macerate the skin more than boric-acid ointment gauze which has been wiped almost free of grease. However, even with this precaution, it is best to use only a single layer.

In regard to dressings, it is best to leave fresh grafts a minimum of five days before dressing. Too zealous attention in the way of early dressings can ruin the best graft.

Local antibiotics are not desirable in clean plastic procedures, although prophylactic medications of that nature by parenteral or other routes are of value.

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53 Main Street.

PRESBYOPIA

Comparative observations of white and negro populations

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Several years ago, while serving with the United States Army at Gorgas Hospital, Panama Canal Zone, I had an opportunity to observe some ophthalmic problems of a tropical climate.

Our patients were divided into two main categories: (1) "gold" and (2) "silver." This segregation was initiated during the years of the construction of the Panama Canal. Because of adverse health and climatic conditions, large numbers of laborers were imported from Jamaica, the West Indies, and the Republic of Panama. They were paid in silver; whereas, the "Norte-Americanos" were paid in an equivalent weight of gold. Today this segregation still exists, so that both "gold" and "silver" wards, clinics, and patients are distinguished. With few exceptions, however, the medical facilities and personnel for both groups are equal in caliber.

It was soon apparent that significant differences occurred in the prevalence of various diseases seen in the "gold" clinics as compared with the "silver" clinics; for example, lues and tuberculosis were more common in the "silver" clinics.

In the Medical Department, Scrimshaw, Culver, and Stevenson investigated the incidence of hypertension in the two classes and reached most interesting conclusions as to the factors involved. It appears from their most careful studies that psychologic and social factors were the predisposing causes of hypertension, rather than diet, race, or the more commonly observed differences. The imported Jamaican, particularly those of the second generation, deprived of rights of citizenship and unable to return to his native land, is easily a prey to psychosomatic difficulties, with presumably secondary organic changes.

My interest was, naturally, greatest in the ophthalmic problems, and this brief paper is chiefly concerned with observations in refraction.

Among the refractionists working in "gold" and "silver" clinics certain empirical observations were noted:

1. Presbyopia seemed to develop at an early age among the "silver" patients.
2. The course of development was rather abrupt, with early requirements of additions of +2.5D.
3. "Silver" patients desire bifocals and have no difficulty in adjusting to their use.
4. "Silver" patients enjoy the wearing of lenses, gaining respect in their social life thereby, and often will malinger in the attempt to acquire this new object of prestige.

On the basis of the above clinical impressions several thousand clinical records were analyzed. The records consisted of refractions performed during the years 1935 to 1945 and, in addition to my own examinations, included those performed by other competent ophthalmologists.

Tables 1 and 2 are comprised of 25 samples, each, taken at random from this large number of records.

Discussion

The complete explanation of the mechanism of accommodation is not known. It is generally accepted, however, that loss of accommodative power, as occurs in presbyopia, is due to a decrease in the mobility of the lens substance. This is quite opposed to the weakening of the ciliary muscle occurring during the course of acute infectious diseases, particularly diphtheria. We have long known clinically that such factors as general debility, chronic systemic diseases,

and occupational stress may accelerate the onset of presbyopia.

Among the physical differences in our Negro and white population in Panama the following may play a role in the explanation of their presbyopic differences:

1. The low incidence of myopia in the Negro's examination, with the subsequent increase in emmetropia and hypermetropia.

2. A possible climatic factor. The number of cases observed among "gold" patients who had spent their entire lives in the tropics is too few to permit drawing conclusions, but the tropical climate may well predispose to lens sclerosis.

3. There was a possibility that the accuracy in age as given by the Negroes might be subject to doubt, but a sufficient number of established cases would tend to rule out this error.

4. The higher percentage of degenerative diseases, such as lues and tuberculosis, in the "silver" population is probably another factor in the early onset of presbyopia.

5. Studies in diet and food habits of the two classes showed no significant difference. Despite economic differences the tropical natives are abundantly supplied with natural foods easily obtainable.

TABLE 1

PRESBYOPIC ADDITIONS AMONG "SILVER" PATIENTS

Case No.	Age (years)	Addition (diopters)
1.	75	+2.75
2.	54	+2.50
3.	42	+1.25
4.	50	+2.50
5.	54	+2.50
6.	42	+1.25
7.	43	+1.25
8.	51	+2.00
9.	48	+2.25
10.	47	+2.50
11.	52	+2.50
12.	60	+2.75
13.	35	+3.50
14.	51	+2.50
15.	59	+2.50
16.	44	+1.00
17.	37	+1.50
18.	43	+1.50
19.	52	+2.25
20.	47	+2.50
21.	43	+2.25
22.	57	+2.50
23.	49	+2.50
24.	41	+2.00
25.	59	+2.50

TABLE 2

PRESBYOPIC ADDITIONS AMONG "GOLD" PATIENTS

Case No.	Age (years)	Addition (diopters)
1.	44	+1.50
2.	45	+1.00
3.	37	+0.75
4.	57	+2.25
5.	40	+1.50
6.	63	+2.50
7.	48	+2.00
8.	46	+1.75
9.	48	+1.50
10.	55	+2.50
11.	40	+1.00
12.	53	+2.50
13.	45	+2.00
14.	41	+2.00
15.	40	+1.50
16.	47	+1.50
17.	47	+2.25
18.	50	+2.25
19.	49	+1.50
20.	41	+1.50
21.	50	+1.75
22.	55	+2.25
23.	67	+2.50
24.	70	+1.75
25.	65	+2.50

SUMMARY

It has been established beyond doubt that the Negro population of the Panama Canal Zone develops presbyopia from 5 to 10 years earlier than the white population. The presbyopia occurs abruptly. The usually accepted causes, other than the higher incidence of lues and tuberculosis, do not seem to afford an explanation of these differences, but social inequality and personal insecurity may well be of fundamental importance in setting off the organic changes within the lens.

This phase of the problem certainly deserves further investigation.

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ABDUCENS PARALYSIS IN BRUCELLOSIS*

Report of two cases

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Since the abducens nerve is one of the most commonly affected cranial nerves, it has received considerable attention on the part of the ophthalmologist, otolaryngologist, and neurologist. Its anatomic course through Dorello's canal is long and complicated and presents many possibilities for mechanical compression, stretching, and infection from adjacent structures. The importance of the canal, which is formed by the posterior clinoid process, the tip of the petrosa, and Gruber's ligament, cannot be overestimated, not only in infections of the temporal bone but, as was pointed out by Houser,[1] in infections of the paranasal sinuses as well as in other conditions such as increased intracranial pressure, spontaneous subarachnoid hemorrhage, and trauma. In the majority of cases the causes of unilateral paralysis of the abducens nerve may be determined without difficulty.

The more common causes of paralysis of the abducens nerve are: intrapontile tumors and vascular lesions; meningitis, tumors, abscesses, injuries, and vascular lesions at the base of the brain; localized meningitis (Gradenigo's syndrome) at the petrous apex and petrositis; lesions of the cavernous sinus and orbit; increased intracranial pressure and myasthenia gravis.

Paralysis of the abducens nerve is occasionally observed after spinal anesthesia. Its occurrence in this connection has not been satisfactorily explained. Paralysis may also occur as the result of disease of the sphenoid and ethmoid sinuses. Occasionally, paralysis follows injection of alcohol into the sphenopalatine ganglia for the relief of the so-called Sluder's neuralgia.

Finally, one encounters isolated unilateral paralysis of the abducens nerve of unknown etiology terminating in recovery. Nine such cases were reported by Yaskin[2] in 1939. Since then this author has had seven additional cases. In none of these patients was there any antecedent history of acute infection or trauma—nor was there any evidence of syphilis or other chronic infection, intoxication, or diabetes. Complete studies of the cases failed to reveal any anatomic or chemical causes for the paralysis and spontaneous recovery took place within two weeks to several months.

The absence of an etiologic factor in these cases suggests an analogy to Bell's palsy, the cause of which is likewise obscure. In some instances the cause may be a neuritis due to exposure; in others it may be of a nuclear type possibly due to a virus infection.

Just as Bell's palsy is attributed by some investigators to a lesion of the bony canal in the temporal bone, so one may conceive of a similar causal factor in Dorello's canal in cases of so-called idiopathic abducens paralysis. However, it should be borne in mind that idiopathic abducens paralysis is rare while the so-called Bell's palsy is extremely common.

It is desirable to arrive at an etiologic diagnosis of disease whenever possible. It is for this reason that isolated abducens paralysis occurring in two patients suffering from brucellosis was deemed worthy of report.

Report of cases

Case 1

History. R. H. W., aged 46 years, a real estate broker, with a negative family and past medical history, was admitted to the Graduate Hospital, service of Dr. G. M. Piersol, on October 21, 1941, with the chief complaints of chills, fever, weight loss, and

* From the Departments of Neurology and Medicine, Graduate School of Medicine, University of Pennsylvania. Presented before the Section of Ophthalmology of the College of Physicians of Philadelphia, January, 1949.

marked weakness. The patient had had malaise off and on since midsummer and for 2 or 3 weeks prior to admission to the hospital he had had fever and profuse sweats, losing weight rapidly.

Physical examination. The only findings on physical examination were those of bronchitis. The neurologic examination disclosed slight nuchal rigidity, a suggestive Kernig, and considerable apathy. In the course of three weeks he became progressively worse reaching a state of low-grade delirium with incontinence of urine and profound asthenia. His fever continued between 100°F. and 103°F. with a corresponding rise in pulse rate. It was accompanied by a few slight chills and persistent severe sweats.

Routine urinalysis and blood count revealed nothing of significance. The blood sugar and urea nitrogen were within normal limits. The blood Wassermann was negative. Repeated blood cultures were negative. Studies of the spinal fluid were negative.

It was not until the middle of December approximately three months after the beginning of his illness, that the blood agglutination studies indicated the case was one of brucellosis.

Course. Improvement in the patient's condition occurred and he was discharged from the hospital on January 1, 1942. During the following six months he suffered from weakness and occasional excessive perspiration but was able to carry on his work in a satisfactory manner.

In October, 1942, one year after his illness began, he suddenly developed double vision. This was shown to be due to paralysis of the left abducens nerve. Complete neurologic examination at the time was otherwise negative. The patient's general condition was satisfactory and he made an uneventful recovery in the succeeding few weeks. The agglutination tests were still weakly positive.

Case 2

History. G. O., aged 39 years, a service manager, suddenly developed, on June 17, 1947, occipital headache, nausea, and pain between the shoulder blades which confined him to bed for 10 days. He then developed double vision on looking to the right. One week later the headache improved but he still had double vision.

A somatic and neurologic examination at the time was negative except for a fairly complete right external rectus paralysis. Dr. C. McClure, the referring physician, stated that the spinal fluid studies were entirely negative. X-ray examinations of the skull, thorax, vertebral column, and colon were negative. Electrocardiographic studies showed no abnormalities. Routine blood count and urinalyses were negative. Blood sugar, urea nitrogen, and uric acid values were normal. The blood Wassermann was negative. Agglutination tests made for Brucella abortus were positive in dilutions up to 1:640.

The patient made a satisfactory recovery in the course of the next few weeks.

Discussion

The two reported cases had isolated involvement of the abducens nerve associated with brucellosis. In Case 1 the infection was severe. The patient apparently did not recover for many months after contracting the disease and did not develop the abducens palsy until several months after his illness had started. The second patient was not severely ill and his abducens palsy apparently occurred 10 days after the onset of his illness.

Except for the brucellosis infection, there was no evidence of any other cause for abducens paralysis in these two cases and the question naturally arises as to whether the infection can be held responsible for the paralysis. We believe it was responsible in view of the nature of the disease and the history of the cases.

As is well known, undulant fever is not a unitary disease. It is quite common in the Mediterranean area where it is known as Malta fever; in this area it is often accom-

panied by neurologic complications, such as meningitis, meningo-encephalitis, and meningomyelitis. Involvement of several cranial nerves often occurs with these complications.

In recent years there were moderately severe epidemics of brucellosis in South America, especially in Argentina, and a good many cases were accompanied by neurologic complications. Barros and Fitte[3] report three cases in which acute meningitis (two cases) and meningo-encephalitis (one case) appeared during the course of infection with Brucella melitensis. Dickson and Roaf,[4] in 1946, reported a case of undulant fever complicated by acute transient attacks of aphasia followed by deafness, tinnitus, and paresthesia.

There are quite numerous reports in the foreign literature of the involvement of the cornea and the uveal tract, of the optic nerve, and less commonly of the third, fourth, and sixth nerves.

In this country neurologic complications of brucellosis have received relatively little attention. DeJong[5] reported a case of right sixth nerve palsy and weakness of the left sixth nerve accompanied by neuroretinitis. A satisfactory review from an ophthalmologic standpoint was made by Green,[6] in 1939, and by Heim,[7] in 1945.

There seems to be little doubt that undulant fever, like many other systemic infections, may affect the nervous system, causing not only gross lesions in the meninges, brain, and spinal cord but also neuritis. Previous generations were familiar with the neurologic complications of such common infections as typhoid fever and diphtheria. In recent years we have recognized the fact that the nervous system may be damaged by such well-known infections as measles, chicken pox, and mumps.

In 1916, Guillaine and Barre described a syndrome affecting principally the roots and peripheral nerves which was found to be associated with cutaneous and other forms of diphtheria and with infectious mononucleosis. It would therefore appear to be reasonable to assume that a systemic infection such as undulant fever may cause not only gross disease of the meninges, brain, and cord but may well produce neuritis as exemplified by the two cases of isolated involvement of the abducens nerves herein reported.

These cases should be of particular interest to the ophthalmologist and internist since they demonstrate that any patient with sixth-nerve palsy of undetermined origin who complains of headache, backache, fever, chills, fatigability, and especially sweats should be suspected of having brucellosis. Proper laboratory tests should then be applied in an effort to confirm such a diagnosis.

Treatment

The treatment of brucellosis unfortunately is in an unsatisfactory state. There is no specific treatment that can be relied upon. Brucellin, a nucleoprotein filtrate devised by Huddleston,[8] has been effective in his hands. The use of vaccines and serum has been advised at times. Serum might be helpful in the acute stages of the disease, but one frequently does not see the patient then; vaccine, perhaps 6 or 9 months after the disease has presumably begun, might be of value. The combined use of dihydrostreptomycin and sulfadiazine as reported by Spink and others[9] and the use of aureomycin as reported by Spink and others[10] or the use of chloromycetin as described by Woodward[11] appear to provide the most satisfactory treatments available at this time.

Summary and Conclusion

Two cases of isolated paralysis of the abducens nerve believed to be due to brucellosis are reported. Brucellosis may invade the nervous system, cause gross changes in the meninges, brain, and cord, and may cause neuritis of the extraocular nerves.

It is well to consider the existence of brucellosis when unexplained extraocular palsies are encountered.

Rittenhouse-Plaza (3).

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THE EFFECT OF THE EYE PATCH ON ORGANISMS OF THE CONJUNCTIVAL SAC

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The first real development of knowledge about conjunctival flora occurred in the late 19th century. Foote, Eyre, Back, Hauenschild, Axenfeld, and Morax were largely responsible for the early research on the bacterial flora of the conjunctiva. Foote[1] found that the normal conjunctival sacs were free of organisms in most cases. Eyre[2] found that the conjunctival sacs which had bacteria were most contaminated in the lower fornix, but were free of bacteria in the upper fornix.

Back[3] and Hauenschild[4] proved that, when microörganisms were inoculated into the conjunctival sac, the bacteria may be found in the nose 24 hours later. Axenfeld[5] and Morax[6] were the co-discoverers of the diplobacillus; they did the first comprehensive research on the bacteriology of the eye.

Pathology

The processes that affect the conjunctiva have three avenues of approach: (1) exogenous, (2) endogenous, and (3) by local disease. In general, a pathologic process of the conjunctiva does not differ from that of the mucous membranes. However, since the conjunctiva is continuous with the corneal epithelium, frequently these processes have serious visual effects.[7]

The entire conjunctival membrane secretes mucus—it may, indeed, be considered a superficial gland. Duke-Elder[7] believed that, in the majority of cases, infection from pathogenic organisms was exogenous—by contact, air borne, or from surrounding skin. The conjunctiva is a cubical epithelium. With interruption of the normal mucous secretion of the epithelium, the conjunctival epithelium assumes the characteristics of skin.

Although Foote and Eyre considered the conjunctival sac to be free of organisms, Lindner[8] and Pillat[9] denied this, maintaining that practically every conjunctiva exhibited some bacterial flora.

A wide range of organisms was found in the normal sac, the most common were B. xerosis (100 percent), staphylococcus (94 percent), pneumococcus (41 percent), and Hemophilus lacunatus (22 percent).[9] Staphylococcus albus epidermis was found in greatest numbers at the margin of the lower lid, and contamination ceased if organisms were made to disappear from the lower lashes.[10]

Procedures of culturing the conjunctiva

Elschnig and Ulbrich[11] found that the best results in studying flora of the conjunctiva were obtained when using horse serum and bouillon. These were mixed, and then the mixture was dropped into the lower cul-de-sac. The fluid was then aspirated into a pipette to be delivered on a Petri dish for incubation. Bacterial growth became manifest in 24 to 48 hours. Fifty percent of the cases showed pneumococcus and streptococcus by their method, which had shown no bacteria by smear method alone.

S. Hanford McKee[12] stimulated tear flow by rubbing the lid against the eye. The lacrimal fluid was then collected by a pipette from the inner canthus for incubation on blood-agar plates. His conclusion was that, although the smear may be negative, further bacteriologic investigation may reveal pathogenic organisms. The presence of either streptococcus or pneumococcus may be easily demonstrated in 24 to 48 hours.

TABLE 1

Control Group Colony Count

Patients	First Culture	Culture 24 Hrs. Later	Ratio
1	0	0	
2	0	0	
3	0	0	
4	1	0	
5	0	2	
6	0	0	
7	22	5	
8	16	4	
9	0	0	
10	2	0	
11	0	0	
12	1	0	

Lindner[8] and Jona,[13] after rubbing a portion of the conjunctiva and removing the superficial layers of the epithelium, took smears and cultures of the underlying scrapings. They concluded that, in the beginning of a conjunctival inflammation, the bacteria were impossible to find on a smear because the bacteria were few in number and were present in small clusters on the surface epithelium. They felt that, in the later stages of conjunctival inflammation, the bacteria invaded the epithelial cells of the conjunctiva; therefore, a smear could only be taken after superficial epithelial covering had been rubbed away.

TABLE 2

Patch Group Colony Count

Patients	First Culture	Culture 24 Hrs. Later	Ratio
1	5	21	1/4
2	255	500 plus	1/2
3	1	65	1/60
4	135	263	1/2
5	249	1500 plus	1/5
6	0	3	1/3
7	325	292	1/1
8	22	228	1/10
9	20	70	1/3
10	232	232	1/1
11	256	560	1/2
12	256	560	1/2
13	10	1	1/0.1
14	2	56	1/28
15	30	94	1/3
16	3	82	1/27
17	203	1466	1/7
18	21	726	1/34
19	108	318	1/3

Procedure followed in this experiment

Patients were selected who had, from external gross appearance, a normal conjunctiva; no pus could be expressed into conjunctival cul-de-sac from pressure on the tear-sac area. The patients were divided into a control group in which no patches were used (table 1) and a group in which patches were to be worn (table 2).

With sterile technique, 0.5 cc. of saline solution was instilled into the temporal side of the lower cul-de-sac of each eye to be tested by means of a cotton tipped pipette. The saline remained in the sac for five seconds, with the patient's head tilted in such a way as to retain the solution on the temporal side. The saline was then drawn back into the pipette, great care being taken not

to touch the lid edges or the lashes. Plain broth, previously heated until liquefied, then cooled to 52°C., was then poured into a Petri dish, after the saline had been deposited in the dish. The pour plate was then gently agitated until the culture hardened.

In the control group (table 1) the same procedure was repeated 24 hours later. For the patch group (table 2) the same procedure was used in taking a culture before and after the wearing of a sterile eye dressing for 24 hours.

The Petri dishes in all cases were incubated for 48 hours, then bacterial colony counts were done with a magnifying glass. Errors in counting of plus or minus 50 colonies, when over 200 colonies of growth were present, were considered because of the closeness of the colonies to each other. The most common organisms present on the plates were Staphylococcus albus and Staphylococcus aureus. Differentiation of the bacteria and the bacterial colony counts were done by a pathologic laboratory.*

Comments

The normal conjunctiva was practically never free from microörganisms as is shown under the heading of first cultures (taken on the 31 patients) in Table 1 and Table 2.

The control bacterial colony counts (table 1) showed that the number of colonies vary from day to day. In the patch group, two patients (No. 7 and No. 10) showed no change in colony count after 24 hours of patching and, for some unexplainable reason, one patient (No. 13) showed a decrease in the number of bacterial colonies with the use of the patch. The average ratio of colony count before the patch to 24 hours after the patch was one to three.

Patients, who had their eyes covered, voluntarily complained of itching and stickiness after the eye dressing had been worn for 24 hours. Those symptoms might have come as the result of the proliferation of the bacteria.

Conclusions

1. In a series of 19 cases, the eye patch increased the bacterial colony count in 16 cases.

2. In these experiments Staphylococcus albus was the most common bacteria found and Staphylococcus aureus was the second most common bacteria found.

3. A patch test with the proper method of culturing the contents of the conjunctiva could be of great value in noting conjunctival bacterial behavior before performing intraocular operations.

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* Dr. Paul Gross, Pittsburgh, Pennsylvania, supplied the culture media and did the bacterial colony counts in this experiment.

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NOTES, CASES, INSTRUMENTS

RAPID LENS CHANGES IN DIABETES MELLITUS*

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It is well known that in diabetes mellitus rapid and extreme changes in the refractive condition of the eye occur, and these changes, more frequently than not, are reversible. Diabetic cataracts, outstanding among the lens opacities dependent upon metabolic or endocrine disturbances, have been striking for the rapidity of their development. Although these facts are well known, it is easy to lose sight of the extreme degree of change which the lens can undergo within a short time in diabetes and especially to lose sight of the fact that advanced changes may sometimes completely regress.

Bellows[1] has summarized both the common refractive changes which occur with diabetes mellitus and the information which is most widely accepted with regard to diabetic cataract.

Among the transitory refractive changes three are outstanding: (1) Development of an increased hyperopia with a need for stronger convex lenses. This is especially prone to occur with an improvement in the general condition of the patient and a lessening of the glycosuria. (2) Development of weakness of accommodation, especially in the younger diabetic patients. (3) Myopic change, which is much less common than hyperopic change and is found chiefly in cases with a high blood sugar and glycosuria. Myopic change in adults should arouse suspicion of diabetes.

Cataracts are a more serious and less frequently reversible lenticular complication of diabetes. There is still much disagreement as to the accurate classification of true diabetic cataracts, and there are some who would limit the term not only to lens opacities of characteristic morphologic type and clinical course, but also to those occurring in the younger diabetic patients. In general, the age group for this lens change is from young childhood to about the age of 40 years, although cases of opacities which seem to be diabetic in origin have been described in patients whose ages range from 11 months to 49 years.

Although it has been experimentally proved on laboratory animals that pancreatic deficiency may cause cataracts, the exact cause and the mechanism of formation of true diabetic cataracts are still not known. It seems unlikely that these opacities form either as a direct action of the increased sugar content in the blood or aqueous or as the result of osmotic variations which occur with hyperglycemia. A somewhat more likely theory is that toxins which affect the lens material result from the disturbed metabolism in diabetes.

The clinical appearance and course of diabetic cataract are well known.[2-4] Outstanding among the features of this cataract are its very rapid development and growth. It is well known that these lens changes may progress from clear lens to complete opacification within a relatively few hours and that characteristically the cataracts mature within a few months.

The treatment of diabetic cataract is somewhat difficult to evaluate, especially since the course which the cataract may follow is by no means constant. However, it appears that vigorous insulin therapy in the early stages of the development of the diabetic cataract may delay or stop its progress; although rarely, regression of diabetic opacities has been reported. Perhaps there is no better proof that a lenticular opacity is diabetic in origin than the fact that it is influenced by insulin administration.

The case under discussion in this paper is striking in that, after very rapid develop-

* From Department of Ophthalmology, Bowman Gray School of Medicine.

ment of a moderately advanced diabetic cataract, regression was complete and equally rapid with the patient under therapy with globin insulin. It is also unusual in that the opacities developed and regressed during the period of rapid fall of blood sugar with regulation of an acute exacerbation of a mild diabetic, whose subsequent course suggests that she should be classified among the cases of so-called "acute" diabetes.

Case report

History. This 48-year-old white married woman was admitted to Baptist Hospital on March 11, 1949, for study and regulation of what, by her story, appeared to be diabetes mellitus. She had been in the hospital on two previous occasions—the first in August, 1941, at which time she had an essentially uneventful delivery of a male child.

Her second admission was in September, 1943, at which time she complained of a lump in her right side which had been steadily growing while the patient lost about 15 pounds over the period of six months. Studies on that admission revealed the presence of a retroperitoneal mass outside the colon and kidney on the right side which was diagnosed as a retroperitoneal lymphosarcoma. Although, at that time, it seemed that her prognosis was bad, she was given deep X ray therapy (6,216 r, in divided doses). The mass regressed in size, and the patient had been essentially free of symptoms up to the present admission. On both of these first two admissions the patient had complete laboratory studies, and her urine was sugar free and her kidney function was good.

At the present admission the patient had the classical symptoms of diabetes mellitus, including polyphagia, polydipsia, polyuria, repeated superficial infections, and a weight loss of 25 pounds within the past few months. She had noticed this symptom complex for six months before admission. She had recently seen her family physician who, finding that she had sugar in her urine, had placed her on a low carbohydrate diet. In addition, the patient stated that she had noticed a very marked change in her vision within the past few weeks. She had had her present glasses for five years but had been quite satisfied with them until the past 2 or 3 weeks, during which time she had become unable to read with them at all. She could see at a distance through the reading segments better than through the distance portion.

The ocular condition showed a rather startling course. On the second hospital day the patient was seen because of her recent marked visual loss and at that time was found to have vision of: R.E., 20/50−2, unimproved by her glasses; L.E., 20/200, improved to 20/50−2 by her old glasses, +0.5D. sph. ⊂ −0.25D. cyl. ax. 90°, O.U., with a +1.50D. reading addition.

At this time, extraocular movements, pupillary reactions, phorias, and funduscopic examination were all essentially normal. There were early arteriosclerotic changes in the retinal arterioles, but no hemorrhages and exudates, and the lenses and media were entirely clear.

Fogging refraction at this time revealed: R.E., improved to 20/15, with a +3.5D. sph. ⊂ −1.0D. cyl. ax. 105°; L.E., improved to 20/15, with a +3.75D. sph. ⊂ −1.0D. cyl. ax. 80°; and +1.5D. reading addition, O.U., gave a most satisfactory reading distance of 36 to 38 cm.

In view of the very marked change in the patient's lenses, it was felt unwise to give the patient the prescription which she took at this time, and it was decided to check her again after her diabetes was better regulated. Consequently she was again seen after four days of globin insulin therapy, at which time her urine was sugar free and her blood sugar below 200 mg. percent.

At this time she told us that she had had extreme loss of vision just since the visit to the eye clinic a few days before, and that it was just as though a veil had come before her eyes so that she was unable to read anything at all or to see clearly through the upper or lower portion of her old glasses.

Examination at this time showed a striking change which had taken place in the few days since the last examination. The patient had developed bilateral, rather advanced lenticular opacities of the posterior subcapsular type. The opacities were somewhat brownish, granular, saucer-shaped cataracts with very jagged, irregular margins. Only a very few vacuoles were noted at this time. At this time it was impossible to improve the patient's vision above 20/100 with any lenses which could be given her.

Three days later the patient's vision was again checked and, once again, it was evident that startling changes had occurred within her lenses. The cataract on the left had completely disappeared and on the right there was only a tiny remnant of the posterior subcapsular opacity which had been present three days before. Refraction was: R.E., 20/15, with a +5.75D. sph. ⊂ −0.75D. cyl. ax. 115°; L.E., about 20/15, with a +6.D. sph. ⊂ −0.75D. cyl. ax. 90°. A +1.75D. reading addition, O.U., gave a best reading distance of about 37 cm.

The patient was given this prescription after it was thoroughly explained to her that it was quite unlikely that these glasses would be satisfactory for long with her lenses undergoing such rapid changes, but she was extremely anxious to leave the hospital and to have the glasses so that she could read and do her work. At this time her fasting blood sugar was again within normal limits, and her urine was sugar free. She was discharged from the hospital on 50 units of globin insulin per day, to return for a check-up within a month.

Six weeks after her discharge the patient was seen again and at that time reported that she had been able to reduce her insulin in steps until it was stopped entirely and that she was now regulated on diet alone. At that time her corrected vision had fallen to: R.E., 20/50−2; L.E., 20/100+1. Once again she readily improved to: R.E., 20/15, with a +4.25D. sph. ⊂ 0.75D. cyl. ax. 120°; L.E., +4.0D. sph. ⊂ −0.25D. cyl. ax. 65°. Her lenses were entirely free of any opacities.

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SUBRETINAL HEMORRHAGE SIMULATING SARCOMA OF THE CHOROID*

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An interesting case, under the same title, was reported by Joseph Laval in the January, 1948, issue of the AMERICAN JOURNAL OF OPHTHALMOLOGY. On the left macula lutea of a 48-year-old woman there was a round pigmented tumor which had the diameter of six papillas and protruded for about 5.0D. It was continuous with the upper temporal border of the papilla. The author removed the globe following a diagnosis of melanosarcoma of the choroid. Histologic study revealed a hemorrhage between the retina and the choroid; there was no tumor in the eye, although serial sections had been made.

In commenting on his case, Laval remarks that the hemorrhage occurring at the macula

* From the Ophthalmological Department of the Hospital of the Order of Hospitalers, Budapest.

lutea might have given rise to degeneratio disciformis maculae luteae if the eyeball had not been removed. This presumption was not borne out because, during two years of observation following the operation, no symptom related to that process developed in the right eye in which normal retinal vessels were present. In contradistinction to Laval's case, the patient herein reported later developed disciform degeneration at the very place of the hemorrhage which had suggested sarcoma.

Fig. 1 (Lugossy). The fundus of the right eye of a man, aged 74 years. On the macula lutea, there is a prominent dark-gray area (sarcoma?) below the detached retina.

Fig. 2 (Lugossy). The same fundus, as shown in Figure 1, one year later.

Case report

History. V. J., a man, aged 74 years, suddenly lost the sight of his right eye while reading four days previously. The sight of his left eye had always been poor.

Examination. The right eye was apparently normal, the refracting media were clear. The retina was, aside from the upper-inner quadrant, detached, fluttering, forming several folds and projections. The detachment extended along a semicircle to the papilla. There were pool-like hemorrhages along the elevated retina especially above the papilla; they were subretinally situated. The vessels were very narrow. There was no objective sight. The localization of light was good. Tension was 8 mm. Hg (Schiøtz).

The anterior part of the left eye was intact. The refracting media were clear. On the fundus there was, at the region of the macula lutea, a grayish white degenerated area the diameter of several papillas. Some small pigmented spots were seen within this area. The vessels were narrow with rigid walls. In addition, fine pigment dissemination and gross pigment were seen, especially below. Vision was: finger counting at 0.5 m. Tension was 15 mm. Hg (Schiøtz).

While the patient was staying in the hospital, the retina became partly reattached. Then we became aware of a large, flat, prominent (about 8.0D.) area below the upper projection. This prominent area was dark gray (sarcoma?). Thus the lower detachment was merely a sequel (fig. 1). On the second week the vitreous became gradually turbid, yielding no red reflection. The patient left the ward. He was told to return if he had pain.

The patient reported one year later. The right fundus could be examined again with the ophthalmoscope. On the right macula lutea there was a degeneration resembling that of the left eye (fig. 2). Vision was: right eye, counting fingers at 1.0 m.; left

eye, counting fingers at 0.5 m.

No doubt, we were right when we did not insist on operation. The short history, the sudden deterioration of sight, the loose detachment of the retina (contrasting with the tight detachment observed when a tumor is present), the low tension, the age of the patient, all spoke against enucleation.

On diaphanoscopy there was a shadow everywhere but below. One year later, however, the degeneratio disciformis maculæ lutæ observed in the right eye also demonstrated that the tumor imitating sarcoma was a subretinal hemorrhage only.

H. Zsigmond u., 17-19.

MERCURIALENTIS

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Mercurialentis was first noted in 1943 by Atkinson[1] who described "a colored reflex from the anterior capsule of the lens which occurs in mercurialism." This reflex, coming from the anterior capsule of the lens, was described as lusterless and homogeneous. It was located somewhat deeper in the pupillary zone. The color varied in different individuals, from a light brownish-gray to a deep rose-brown. Small, round, punched-out defects appeared in the reflex. Although the reflex appeared fairly dense, there was no disturbance of the red reflex upon ophthalmoscopic examination. This brown reflex was believed to be due to the deposit of mercury on or in the anterior capsule of the lens. The capsular reflex did not disappear when the patient was removed from the mercurial environment, for it has been observed even 20 years after cessation of mercurial exposure. Atkinson also observed a similar reflex from the anterior adult nuclear zone but from no other ocular structure.

In 50 percent of the cases examined by Atkinson, positive lens changes were found, although in some of his cases there was subclinical mercurialism. Lens changes may be an early manifestation of mercurialism, since heavy metallic "ions" of even low saturation tend to become deposited in lens substance.

Fisher[2] states that he perceived a "dark yellow-brown regular pattern of pigment stains just subcapsularly." Examination of both eyes of his patient was otherwise negative. The patient's history showed that he had rubbed yellow mercuric ointment into his skin several times a day for many years. Fisher, in retrospect, recalled that years earlier he had experimentally produced this same condition in puppies by applying "gray salve" in an attempt to demonstrate heavy metals in the tissues of the eye.

In 1947, Abramowicz[3] reported a case of mercurialism involving the eye in a 57-year-old woman who had received mercurial inunctions for a marginal blepharitis over a period of 10 years. Mercury, ranging from 1.0 to 6.6 percent, had been rubbed into the lids of each eye almost nightly for this entire period. The massage eventually produced a dark bluish-gray discoloration of the skin of the lids. Throughout the bulbar conjunctiva there were many dark bluish patches. Under slitlamp examination these patches appeared to surround the lymphatic tissues. At the extreme periphery of the cornea, Descemet's membrane resembled a thin greenish-gray line. A dull brownish-yellow deposit was described upon the anterior capsule of the lens. However, this was limited to the axial area of the lens and was associated with a senile exfoliation of the lower pupillary border. The patient was given various ointments for many months, but there was no apparent improvement in the condition.

CASE REPORT

Mr. W., aged 78 years, was examined on December 17, 1947. His chief complaint was gradual visual deterioration especially of the left eye of six months' duration. The past eye history was essentially negative. The patient had a diabetic condition about which he had learned five years ago. Six years earlier he had had an intestinal operation—a resected mass had been reported as malignant.

For 37 years, this man had been a hatter, although he has been retired for the past 10 years. At his work he had been constantly exposed to mercury, since it was necessary for him to keep his hands immersed in a solution containing mercury during most of the day. Laboratory findings were negative.

Fig. 1 (Rosen). Slitlamp appearance of the left eye in a case of mercurialentis.

Slitlamp examination. The pupils were widely dilated. A questionable yellowish glow appeared to be present from the endothelial surface of the wide corneal beam, adjacent to the limbus. In the sclera of the right eye there were two areas of small pigmentlike groups of a grayish-brown color. The anterior surface of the lens presented a beautiful pinkish, coppery reflex covering its entire surface right to the periphery. This surface coating was extremely thin and highly metallic causing many highlights and reflections. The coloration appeared to be upon the surface or just below the surface of the capsule. No cellular deposit could be seen in the anterior chamber.

Under the high power of the microscope, this metallic deposit seemed to consist of very small particles crowded together with a suggestion of normal areas between. There was no indication of a sunflower cataract or any other lesion of the anterior capsule.

Other changes, however, were present within each lens consisting of peripheral cortical spokes, nuclear sclerosis, and congenital "riders." The metallic deposit did not disturb the view of the fundus, which could be observed quite readily.

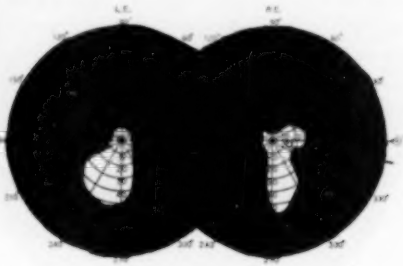

Fig. 2 (Rosen). The visual fields were striking.

The posterior capsule of each lens was checked very carefully both under high power and also in the zone of specular reflection, but no abnormality was observed in this region.

The deposit upon the anterior capsule of the lens was not unlike that seen in both chalcosis lentis and argyrolentis[4] (fig. 1). The fundus showed several pinpoint spherical hemorrhages characteristic of diabetic retinitis. On the retinal surface there were also several small round areas of a metallic-like deposit from which there was a pronounced reflection.

The nerveheads showed definite atrophy of the primary type with a suggestion of a yellowish tint. The visual fields were very striking (fig. 2).

692 High Street.

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CONJUNCTIVAL TRANSPLANT FOR THE TREATMENT OF PTERYGIUM

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It is my opinion that, with the exception of the inner part of the bulbar conjunctiva which differs from other conjunctiva, conjunctival ingrowth is the chief cause of pterygium. It is, therefore, essential to keep the conjunctiva from creeping back onto the cornea after the removal of a pterygium. To accomplish this it is necessary to erect a barrier between the incision for the removed pterygium and the cornea. For this purpose I use the upper and outer part of the bulbar conjunctiva for transplantation, since it is well known that a pterygium never develops from this area.

After thorough scraping and cleansing of the pterygium wound, a conjunctival graft, about 5 by 5 mm. in dimension, is cut and placed at the recipient site. It is not necessary to suture either the donor site or the graft, but the patient should keep his eyes closed for 10 to 15 minutes after positioning of the graft to insure its staying in place.

Before the eye is bandaged, care must be taken to see that it is kept closed. The first postoperative dressing is two days later.

It is surprising how quickly the eye heals after this procedure. By the third or fourth day, there is little redness or injection. The donor site is frequently more inflamed than the eye itself. Healing may be speeded by the use of an eye bath.

On two occasions (out of more than 50 operations) the transplant has become necrotic and caused severe reaction. I do not know whether the graft was inverted before it was placed, or whether necrosis was due to a local anaphylactia.

This method of conjunctival transplantation should prove useful in plastic repair of trachoma, epibulbar carcinoma, posttraumatic pterygoids, and recurrent pterygia. Altogether I have done 50 conjunctival transplantations according to this technique without a recurrence. By using the outer part of the bulbar conjunctiva, one is also able to avoid the conspicuous graft of buccal mucosa. The cosmetic result with my procedure is excellent.

Eötvös-u. 17.

CORRECTION NECESSARY IN PRINCE'S RULE

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Most ophthalmologists measure the power or amplitude of accommodation by the use of the Prince rule or the Berens accommodation meter. In both of these instruments the near point is determined by sliding the target in toward the eye until it begins to blur. The position of the nearest point at which the print is still clear (marked in cm. and inches) is noted, and, alongside, the amplitude in diopters corresponding to this distance is given. The amplitude, as marked on the ruler, is found from the near point by dividing the distance, in cm., into 100. Thus, if the near point is 16 cm., the amplitude is 100 divided by 16, which gives 6.25 diopters.

Beach[1] and all books on refraction teach that before finding the near point of accommodation the eyes must be refracted and made emmetropic. The near point must be found with the correcting lenses before the patient's eye. But when the patient wears his correcting lenses, the amplitude, as shown on the Prince rule, is not the true amplitude in diopters.

Pascal[2,3] has shown that there is a unit of accommodation for every corrected ametrope and that this unit is more than one diopter for the corrected hypermetrope and less than one for the corrected myope.

There are several formulas for this unit, but a very close approximation is that the unit is equal to $1 + 2dL$ diopters, "L" being the power of the lens worn by the patient and "d" the distance in meters between lens and

eye. For the usual position of the correcting lens, the whole system simplifies to adding four percent of L or deducting three percent of L. Thus, if L is plus (corrected hyperope) the unit is 1.00 plus 4/100 of L. If L is minus (corrected myope) the unit is 1.00 minus 3/100 of L.

For example, in a 4.0D. hypermetrope, the unit is 1.00 plus 4/100 of 4.00, equals 1.16D. In a 4.0D. myope, the unit is 1.00 minus 3/100 of 4.00, equals 0.88D. The near point gives the number of units of accommodation the patient has. So that, if the near point on the Prince or Berens rule is 16 cm. the patient has 6.25 units of accommodation. This is derived by dividing 1.00 by 16.

The value of the accommodation in diopters is equal to 6.25 times the value of the unit. In the case of the 4.0D. hypermetrope the accommodation is 6.25 times 1.16, which equals to 7.25 diopters. In the case of the 4.0D. myope this equals to 4.00 times 0.88, which equals to 5.50 diopters.

It can be seen from these two illustrative cases that the dioptral number on the rule, which is 6.25 at 16 cm., is not correct for the patient whose amplitude is determined while he is wearing his glasses. The ophthalmologist, who wishes to know the true amplitude of accommodation of his patient, must find the near point, which gives the number of accommodative units, and multiply this number by the dioptral value of the unit.

66 Main Street.

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COSMETIC CURE OF ALTERNATING SQUINT*

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At the outset, I wish to make it clear that the type of case to which I am referring has been given up by the orthoptist without any hope of treatment producing simultaneous macular perception. The case may be one with or without refractive error, and the vision with or without glasses may be 6/6 or 6/9 in each eye. The patient usually has a marked preference for fixing with one eye, but this preference is sometimes absent and he may be equally happy with either eye. We are, therefore, considering the matter of cosmetic cure only.

At the Worcester Eye Hospital during the past few years different operations have been performed with cosmetic cure as their aim, and the object of this article is to attempt to assess their respective values.

Broadly speaking the cases can be divided into two groups: (1) Those with an angle of more than 20 degrees with or without glasses, and (2) those with an angle of less than 20 degrees with or without glasses.

1. In this group, in which the angle is more than 20 degrees, the operation of choice would seem to be that of resection and recession. The procedure at this hospital has been to get an orthoptic report noting the measurement of the angle, and with which eye the patient prefers to fix. The resection and recession operation is then done on the *other* eye, that is, the eye that usually squints. The amount of resection and recession done has been in accordance with the appended table and, if these measurements are carried out at the operation, the results appear to be remarkably accurate.

* From the Worcester Eye Hospital.

Angle of Squint	*Resection in mm.*	*Recession in mm.*
10	7	0
15	7	2
20	7	3
25	8	3
30	9	4
35	10	4
40	10	5
45	12	5

It is the custom of the surgeon to use a pair of dividers to insure accuracy, and latterly the sclera has been marked with gentian violet. This may seem a somewhat rule-of-thumb method, but experience has shown that results are far better than those obtained by guess work.

2. In this group several different operations have been performed, and the following remarks are confined to those cases in which the squint, as measured on the synoptophore, is, say 20 degrees or less without glasses and 15 degrees or less with.

a. Resection and recession. This operation is good but is a somewhat elaborate one for a small degree of squint. Remarkably accurate results have been obtained in these cases when checked up by a postoperative orthoptic report.

b. Single recession. In a small group of cases the operation of recession of the internal rectus was performed without interference with the externus. The average improvement in a series of 11 cases was seven degrees only. This series showed a tremendous variation, from 1 to 21 degrees. In this small series, nine cases out of 11 had an eventual improvement of less than eight degrees. I would, therefore, regard this operation as unreliable.

c. Double myotomy. In a series of 13 cases, the average improvement was 10 degrees, and the greatest improvement noticed was 16 degrees. This improvement in a squint with a maximum of, say, 20 degrees without glasses, or 15 degrees with, is the equivalent, in most cases, of a cosmetic cure.

I consider this operation a neglected one and, in view of the encouraging results obtained and simplicity of the operation, brief mention of the operative details will be made. It was first described by Chavasse in the *Transactions of the Ophthalmological Society of the United Kingdom*, volume 54, page 506, 1934.

Briefly the details are:

An incision is made in the conjunctiva over the internal rectus and this muscle is thoroughly exposed to a distance shortly behind the equator. I use no clamp to hold the muscle. With de Wecker's scissors the muscle is snipped through, above and below, in the region of the equator, each incision being through about one third of the width of the muscle.

If the degree of squint is a small one, smaller incisions can be made, but it is inadvisable to leave less than one third of the total muscle bulk intact. The bleeding is arrested with swabs soaked in adrenalin, and the conjunctiva is sutured. The same procedure is carried out on each eye.

d. Single myotomy. In a very small number of cases this operation was done, but the results were disappointing and no more than five degrees of improvement was obtained.

I acknowledge, with many thanks, the permission of Mr. I. Lloyd Johnstone to quote from a number of cases which he has operated on. I am also indebted to Miss B. Dolan, the orthoptist at the Worcester Eye Hospital, for much painstaking work, not only in examining the patients reported, but in carefully tabulating the preoperative and postoperative findings with a wealth of detail.

STREPTOMYCIN TREATMENT OF CONJUNCTIVAL TUBERCULOSIS

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Duke-Elder* states that conjunctival tubercles occur mainly in young adults of the second and third decades; the youngest patient was an infant, aged six months; the oldest, aged 76 years. He further writes that

* Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, Mosby, 1944, v. 2, p. 1630.

the prognosis has been difficult to estimate and that the treatment has been either: (1) Radical excision or curettage with subsequent cauterization of the wound, (2) local ultraviolet light, (3) X rays, and (4) antitubercular general treatment.

The favorable response of choroidal tubercles* to streptomycin therapy prompted the treatment with this substance of a proved case of conjunctival tuberculosis.

Report of case

History. The patient, a white woman, aged 30 years, was seen on July 31, 1948. She recalled that six months previously an acid-fast patient coughed in her face. In May, 1948, she observed a localized redness on the conjunctiva of the right lower lid; this became progressively worse—the lid becoming edematous, but was not painful.

Examination of the left eye revealed a conjunctival ulceration, 3.5 mm. in circumference, in the middle third of the lower lid at the sulcus subtarsalis; the adjacent areas were markedly injected, slightly indurated, and edematous. With the slitlamp, the margins of the ulcer were irregular and undermined; the base was covered with a dirty gray exudate; the cornea, anterior chamber, and iris were normal.

Regional adenitis was present; the preauricular and the submaxillary glands were easily palpable but nontender.

Laboratory data showed a negative Wassermann, a normal blood count, and negative agglutination for B. typhosis, B. abortus, and B. tularensae. A biopsy was performed and the pathologic report was that of tubercles with giant cells, epithelioid cells, a round-cell infiltrated zone, and a large central area of necrosis. The diagnosis given was that of tuberculosis of the conjunctiva.

Treatment

On August 7, 1948, streptomycin, one gm. daily in divided doses was administered intramuscularly for four-and-one-half weeks. Topically, 10,000 µg./cc. of streptomycin was instilled into the conjunctival sac every two hours for approximately four weeks. Improvement was gradual, the ulcer becoming progressively smaller, cleaner, and more regular. After five weeks of treatment the ulceration was completely healed.

1330 Union Street.

* Sykowski and Lawrence: Am. J. Ophth., 31:1629 (Dec.) 1948.

A LOW-PRICED ELECTROMAGNET*

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Syracuse, New York

An excellent and powerful electromagnet which is capable of easily removing magnetic intraocular foreign bodies is available at a low price.

The complete outfit consists of a field coil with a central core, a 20-plate Selenium rectifier, three tips, an off-and-on switch, the necessary wiring, and case.

The total magnetic surface is the central core which has a diameter of about that of a dime. Very little, if any, magnetic attraction is exerted by the remainder of the coil surface. Its power is shown by the fact that this small surface easily lifted a 30-pound weight. Figure 1 shows coil, threaded core, and the three tips. Figure 2 shows the core in the proper place fitted with the short blunt tip as well as the rectifier.

The central core, which is easily removable, is 18 mm. in diameter and 28 mm. thick. This has a central opening eight mm. in diameter which is threaded to receive the tips. The front face of the field coil measures 60 mm. in diameter, the back 71 mm., and the thickness 28 mm. With the aid of the rectifier either A.C. or D.C. current (110 volts) may be used.

The tips are steel with nickel plating and are of the three types shown in the illustration. The shortest, rather blunt tip is 27 mm.

* For sale by the Magnetic Specialties Corporation, 25 Park Place, New York 7, New York.

long; the one with the flat surfaces is 36 mm. long with an 18-mm. extension; the other is 42 mm. long of which the protruding end is 28 mm. All are 18 mm. in diameter.

Experiments

Experiment 1. About a dozen pieces of iron wire, one mm. in diameter and varying in length from one mm. to 12 mm., were placed in different positions in the vitreous of a calf's eye through a small scleral incision. Using the various tips, these were all easily removed through the posterior route.

Experiment 2. Again the same number of iron-wire pieces was implanted in the vitreous at varying distances from the lens. Holding the shortest (blunt) tip against the cornea, only two were drawn into the anterior chamber. The tip was then removed, and the flat surface of the core itself was applied to the cornea. The eye could be felt vibrating between the fingers while about

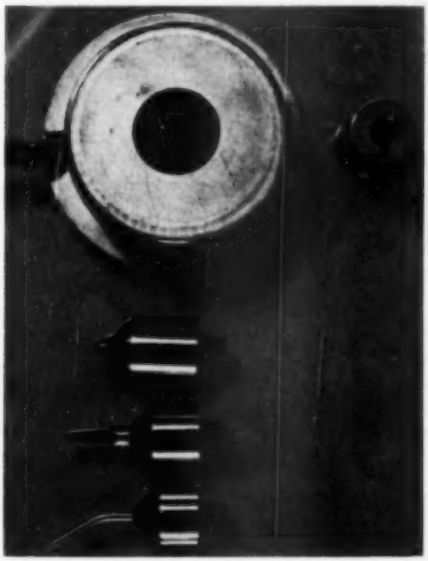

Fig. 1. Shows coil, core and the three tips.

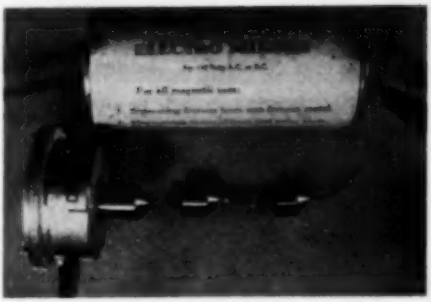

Fig. 2. The assembled magnet, fitted with one tip; also the rectifier.

half of the particles popped into the anterior chamber. Several more were drawn into the anterior chamber by "walking" them from the side around toward the front. Incidentally, the edge of the opening in the core is quite sharp. When it was used flat against the cornea, the surface of the cornea was easily abraded. Therefore, the contact must be very gentle or the core surface must be covered with gauze and held in one place at a time without sliding.

Conclusions

There is now available a low-priced electromagnet which easily removes magnetic foreign bodies through the posterior route. This is usually the preferred way and in keeping with the old dictum of "remove them by the shortest route," especially if the retina and choroid are coagulated by a few punctures on each side of the line of the scleral incision before the latter is made.

For removing foreign bodies through the anterior route, the magnet's capability is uncertain unless the foreign bodies are fairly far forward. However, the diagnostic pull may be of value.

The performance of this magnet compares favorably with that of magnets many times more expensive.

713 East Genesee Street.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

November 7, 1949

DR. SIDNEY A. FOX, *president*

INSTRUMENTS USED IN REFRACTION

DR. BERNARD FREAD discussed this subject during the instruction period.

OCULAR STATUS OF PRESCHOOL CHILD

DR. GEORGE J. EPSTEIN said that the development of effective vision in the infant starts about the fourth month of life with a level of about 20/2,400, has reached 20/130 by the end of the first year, and 20/40 by the end of the fifth or sixth year. Such development occurs in the normal eye, with no sensory obstacles to the acquisition of normal visual acuity. The presence of such sensory obstacles—opacities in the refractive media, major lesions of the retina or optic nerve, marked refractive error—during the first few years of life probably interrupts permanently the development of normal vision.

Binocular single vision develops as a conditioned reflex largely between the sixth month and the end of the second year, with consolidation by the end of the fifth year. Obstacles to such development operative in this period—for example, high hyperopia or myopia, anisometropia, congenital anomalies of the extraocular muscles—may produce strabismus.

The importance of the second and third years of life as the period of acquisition of monocular and binocular vision indicates the necessity for a thorough understanding of the status of the normal eye, and especially its refractive status, during this period. Very little information on this subject is available in the literature.

Eye examinations of 400 normal preschool children, ranging in age from one to three years was performed under cycloplegia with 0.125-percent atropine sulfate solution, after it was found that 0.25-percent atropine resulted in almost 15 percent toxic reactions. This study showed that the bulk of cases (66 percent) were distributed evenly between emmetropia and two diopters of hyperopia. Between 2.25 and 3.0 diopters of hyperopia, there was a rather rapid decline in incidence, and an abrupt falling off occurred above the 3.0 diopter level. There was a precipitate drop in incidence on the myopic side of emmetropia. The mean refraction for the entire group was 1.22 diopters of hyperopia.

Breakdown of the hyperopic individuals into three-month age intervals from 12 to 38 months showed no significant decrease or increase in the average hyperopia of 1.5 diopters. Hyperopic, myopic, and mixed astigmatism (over 1.0 diopter) showed a fairly common occurrence in this series.

These refractive studies were performed on presumably normal children. Those suspected of ocular defects showed the following findings: Strabismus in 21 out of 35 suspected cases; high myopia in three out of four cases of suspected visual defect.

The norms of refraction found in this study are in contrast to existing beliefs, which indicate a hyperopia of from 2.5 to 5.0 diopters at birth, declining gradually to near emmetropia at the age of five or six years.

If the refractive curve found in this series is valid, routine eye examinations of all children soon after the first year may allow us to select cases of potential visual defects and strabismus, marked refractive error of whatever kind particularly, and by application of appropriate treatment (for example, atropine, refractive correction), prevent or

ameliorate defective vision or strabismus in many cases. When defects are irremediable, knowledge of the child's visual status is important to the parents and educators. Dr. Epstein concluded by saying that the prophylactic possibilities indicated further coöperation of pediatrician and ophthalmologist for exploration in this field.

Discussion. Dr. Alfred Cowan said that it is always a difficult problem to refract babies and, therefore, it is easier to criticize the work done on them than to do it yourself. The accommodation in babies has a tremendous range, and it requires a strong cycloplegic to paralyze it completely, and he suggested a strong percentage of atropine. He said that 0.125-percent atropine is not sufficient, but that to use a stronger solution might be dangerous. All findings, therefore, must be considered in relation to the residual amount of accommodation.

Babies usually have a high degree of hypermetropia, about 20 diopters, due to great curvature of the crystalline lens. About 4.0 diopters of hypermetropia in infants is the average norm. Dr. Cowan criticized the division of ametropia into pathologic and nonpathologic. He said that, if two degrees of astigmatism are not pathologic, and one says that 2.5 degrees are pathologic, then one is drawing the line very thin. He said that he does not consider ametropia pathologic nor a disease.

Cardinal points in corrected ametropia

Dr. Joseph I. Pascal said that the correcting effect of plus or minus lenses is due wholly or almost wholly to a displacement of the cardinal points of the eye and not to a change in the total refractive power.

A knowledge of this is helpful in considering changes in the size of the retinal image and indirectly of the ocular image. The size of the focused image of any optical system depends upon the power of the optical system. If the lenses which corrected the ametropia did so by increasing or decreasing the power of the whole optical system by the full power of the lens, changes in image size as a result of the correction would be much more marked than they ordinarily are.

By means of the benzene ring schema, the movements of all the cardinal points occasioned by correcting lenses placed in the anterior principal focal plane of the eye can be easily visualized. The resultant changes in the "thickness" of the optical system, the displacement of the secondary axes, the increase or decrease in the size of the retinal image, can be read off directly from the schema. For this presentation the important set of cardinal points is the "second" set, that is, P_2, F_2, and N_2. They are all displaced forward by a convex lens and backward by a concave lens as indicated in the schema. These movements hold true for all positions of the correcting lens; whereas, the movements of the "first" set of cardinal points are variable and may be ignored.

Discussion. Dr. Kestenbaum asked the question: Why, when the lens is removed, does the patient see with a correction of 10 diopters, when the removed lens had a correction of 20 diopters? Dr. Pascal answered by explaining that the cardinal points had been changed, the principal points had been moved forward toward the cornea and caused a myopia of about −10.0D. The patient loses +20.0D, by removing the lens, and the change in the cardinal points causes a myopia of about −10.0D., thus he is left with a hyperopia of +10.0D.

Clinical management of ametropia

Dr. Alfred Cowan said that, regardless of the number of visits, every refraction can be divided into three stages. In the first stage the procedure is determined. In the second stage the exact static refraction is ascertained. With the exact static refraction and all the data pertaining to the case, it is in the third stage, often called the postcycloplegic examination, when a cycloplegic is used, that the ophthalmologist will determine just how much of the static error should be corrected, the kind of glasses to prescribe,

how and when they should be used, and whether any glasses at all should be given.

It should never be forgotten that, unless lenses will improve the visual acuity or relieve symptoms of asthenopia, they are just a nuisance. It is the duty of the ophthalmologist always to consider very carefully before he prescribes glasses for constant use for anyone, but especially in the case of a child. He should never forget that simple ametropia is not a disease and that no one ever goes blind from it.

Bernard Kronenberg,
Recording Secretary.

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

August 13, 1949

Penetration of globe by fishhook

Dr. Ralph O. Rychener reported a case of penetration of the globe by a fishhook in a man, L.R., aged 42 years, who had lost his right eye in a hunting accident as a child. On July 2, 1949, while rowing a boat for a fisherman who was casting, he was struck in the left eye with the artificial plug. One hook perforated the lower left lid and the globe, making it impossible to separate the lid from the eyeball. An unsuccessful attempt was made at Paris, Tennessee, to incise the lid and deliver the hook. Finally the hook was cut adjacent to the plug and the patient was referred to Memphis with the lid tightly anchored to the globe by the shank of the hook which protruded above the lid approximately two cm.

After several unsuccessful attempts with various instruments, the hook was finally cut off flush with the skin surface of the lower lid with a rib resector. The remaining shank of the hook was then delivered through the lower lid into the lower cul-de-sac. The barb was found to have perforated the globe at the ora serrata and, because of the various manipulations, it had reversed itself so that it was pointed downward and backward into the vitreous.

The sclera at this point was bared and the barb exposed. The wound was ringed with diathermy contacts and enlarged with a Graefe knife and the barb delivered with some uveal tissue which sank back into the globe. There was a large vitreous loss. The sclera was closed with mattress sutures of chromic gut and the conjunctiva closed with plain gut. There was slight traumatic hyphemia and the pupil was distorted down and out.

The patient was kept in bed with a binocular bandage. Penicillin, 300,000 units daily, was administered and atropine instilled at daily dressings. Within a week he stated at dressing that his vision was returning and, although vitreous hemorrhage obscured fundus details, he was able to count fingers at three feet.

The patient was out of bed on the 17th day and returned to his home in three weeks following the injury. Treatment consisted of pinhole glasses, potassium iodide internally, and atropine daily.

On August 8, 1949, visual acuity was 6/15 and J4, improved with a −1.75D. sph. to 6/10 and J3; with a correction for presbyopia. Pinhole glasses were removed.

On August 11, 1949, visual acuity in this left eye was 6/7.5, improved with −0.5D. sph. to 6/6. Near vision was J8, improved with plus 2.0D. sph. to J1. This correction was prescribed in reading glasses. The vitreous had entirely cleared except for a small vitreous hemorrhage in the lower outer quadrant over the area of the injury. The retina was everywhere in proper position, the tension was normal, and the patient was discharged from further treatment.

Bilateral sclerosing keratitis

Dr. James E. Wilson reported Mrs. J. B. W. The left eye was involved first. It was tender, sensitive to light, red in patchy areas, lids swollen, and vision slightly blurred. These symptoms plus severe epi-

sodes of pain continued from February 1, 1949, until she was well on August 29, 1949. The left eye became entirely white and free of pain by May 3, 1949, and then the same process was repeated in the right eye.

Examination of each eye at the height of the disease showed severe episcleritis accompanied by keratitis in the same sector. In each eye the process started at the upper limbus and went all around the cornea counterclockwise. When the circle was completed, the same tissue did not again become involved. Very early in the disease the lesion at the upper limbus resembled a salmon patch.

There were at times a few keratic precipitates and a few cells in the anterior chamber. The vessels at the limbus were superficial but the infiltration appeared deep. At places where the infiltration was deepest and most extensive, the cornea was longer in clearing and, in two areas in the right eye, it did not completely clear. Usually the cornea cleared rapidly as new areas were involved.

Laboratory studies showed a basal metabolism rate of minus three. Kahn and undulant tests were negative. Physical examination and X-ray films of the chest were negative. Ear, nose, throat, and sinuses were normal. Stools showed no parasites. Tuberculin test was mildly positive to 0.001 mg. of old tuberculin. X-ray studies of the teeth showed no infected areas. Routine blood and urine examinations revealed nothing.

During treatment of the right eye she received heat, atropine, and aureomycin solution. For general treatment she received at one time or another, fever therapy, salicylates, syrup of hydriodic acid, and penicillin injections. During treatment of the second eye the same local treatment was used and, when she also developed conjunctivitis, silver nitrate and bacitracin ointment were added. She was given aureomycin by mouth, and fever therapy was used. On July 16, 1949, when the pain was very great and no treatment seemed to be helping, 150 r of X ray were given to the right eye. The pain diminished markedly but the eye did not look any better. About this same time she was found to be violently positive to staphylococcic toxoid and with frequent shots she was brought up to one cc. of No. 2 solution. Improvement was steady and the second eye had cleared up by July 29, 1949. Final vision was 20/20 in each eye.

Divergence insufficiency

Dr. Alice Deutsch reported M. C. D., a white girl, aged 12 years, who came to the office on September 3, 1949, because her mother noticed that lately she had turned her head either to the right or to left side when walking. She had worn glasses continuously since 1941 because of a mild esotropia. She also had had some orthoptic training in 1945. In 1946, she developed diabetes which was controlled with 20 units of protamine-zinc and five units of plain insulin.

When seen in September, 1947, she was using 16 units of protamine-zinc and 16 units of plain insulin. She was also on a fairly strict diet and was well controlled this way. Her refraction under homatropine was: O.D., +1.5D. sph. ⌒ +0.5D. cyl. ax. 70° = 20/25; O.S., +1.5D. sph. ⌒ +0.5D. cyl. ax. 100° = 20/25. On the Maddox-rod test she showed, while wearing her glasses, an esophoria of 4Δ at 20 feet; there was no vertical deviation. At 16 inches she had an exophoria of 4Δ. Her fundi were normal. She had good fusion.

Her reëxamination on September 3, 1949, showed no change in refraction. The media were clear and the fundi normal. Motility was normal. On the red-glass test she had a homonymous diplopia at 20 feet with the greatest disparity in the primary position. There was no diplopia at 16 inches. Maddox-rod test at 20 feet showed 16Δ esophoria, no hyperphoria; at 16 inches, orthophoria. Prism divergence equaled 2Δ; prism convergence, 26Δ.

These findings, namely, esotropia or eso-

phoria more pronounced for distance than near, homonymous diplopia for distance with a maximal deviation in the primary position, and impairment of prism divergence, are characteristic of divergence insufficiency. The decrease of the esophoria when approaching the near point and the reduced prism divergence differentiates this condition from convergence excess; the normal motility and the concomitant type of deviation from abducens paresis.

The mother furnished the information that the child for several days had shown some sugar in the urine (the urine has been checked regularly three times a day for years). She now uses 10 units of protamine-zinc and 30 units of plain insulin. The blood-sugar was checked the day before and found to be 210 mg. percent more than she had ever had before.

LATE RESULT FROM HÜMMELSHEIM OPERATION

DR. PHILIP MERIWETHER LEWIS presented a patient on whom muscle transplants were done five years previously.

Miss L. H., a white woman, aged 25 years, was seen in June, 1944. She complained of her right eye being crossed all her life and that she could not see with it.

Examination showed a high degree of esotropia of the right eye (30 to 50 degrees of arc) with no motion of the right eye outward past the midline. There was no retraction of the globe on attempted abduction. The right eye was amblyopic, the vision being only 1/200. Vision of the left eye was 20/30 and the refractive error was negligible in both eyes.

At operation a powerful medial rectus was found and recessed six mm. A weak, flabby lateral rectus was resected 12 mm., but it was decided then to transplant the lateral halves of the superior and inferior rectus muscles to the stump of the lateral rectus. Considerable reaction and immediate overcorrection resulted but soon subsided, leaving the eye in perfect position which has been maintained for over five years.

HYDROSULPHOSOL FOR BURNS

DR. PHILIP MERIWETHER LEWIS reported three cases treated with hydrosulphosol.

Case 1. A. M., a white man, aged 39 years, got "caustic soda" in his left eye which he washed out fairly promptly. When seen about four hours later, there was extreme congestion and edema of conjunctiva and eyelids. A burn covered the lower two thirds of the cornea and the conjunctiva of the lower half of the eyeball and of the lower lid and fornix. Hydrosulphosol (five percent concentrate) in castor oil was started at once and repeated every two hours. He was hospitalized for one week during which period he showed a steady improvement. Three weeks after the injury, vision had improved from 20/200 to 20/30 plus and his eye appeared almost normal.

Case 2. A white man, aged 26 years, got lime in his right eye while plastering. It was not completely removed for more than an hour at which time there was a superficial burn of the conjunctiva lining the upper and lower lids and the lower half of the globe. The lower half of the cornea was denuded. Hydrosulphosol (five percent concentrate) in castor oil was used every two hours for five days. Recovery was complete and he resumed work in one week.

Case 3. A white woman, aged 46 years, had a severe corneal ulceration which was treated with the usual antiseptics, antibiotics, paracenteses, and all the things commonly employed. The acute symptoms subsided but a sluggish ulceration persisted stubbornly. Her own blood serum was dropped in the eye every two hours for several days with some improvement, after which hydrosulphosol (five percent concentrate) in castor oil was used, alternating with blood serum. It was well tolerated and seemed to stimulate healing.

Daniel F. Fisher,
Recorder for Eye Section.

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THE JUNE MEETINGS

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY

The nineteenth annual meeting of the Association for Research in Ophthalmology, presided over by Dr. Walter H. Fink of Minneapolis, was held at Toland Hall, University of California Medical School, San Francisco, on June 24th and 25th, just prior to the American Medical Association convention. In attendance were over 200 members and guests. Nine papers were presented the first day and 10 the second day. Marked audience interest reflected the high quality of the papers and the variety of discussion offered. The high proportion of papers dealing with biochemical aspects of eye disease was an interesting indication of the rising importance of biochemistry in ophthalmology, but all fields of basic ophthalmology were represented. In keeping with previous programs, the majority of the papers dealt with basic laboratory studies.

H. F. Falls of Ann Arbor opened the meeting with a paper on sex-linked ocular albinism displaying typical fundus changes in the female heterozygote. Paul W. Miles presented an interesting clinical study of flicker-fusion fields in neuro-ophthalmologic

lesions which provoked considerable discussion.

Kenneth N. Ogle and A. deH. Prangen presented a study of fixation disparity in the binocular fusional processes and this was followed by a paper on the effects of cortisone and ACTH on ocular disease by M. J. Hogan, E. P. Engleman, and associates.

G. K. Smelser and V. Ozanics presented an interesting paper on the relation of steroid hormones to the development of experimental exophthalmos, an important contribution and the latest of a long series of their significant studies on this subject.

Ludwig von Sallmann, Z. Dische, and associates at Columbia University reported on the penetration of cysteine and cystine into the aqueous humor and its relation to early radiation effects on the eye, a paper of exceptional interest in this atomic age. This was followed by a report by Z. Dische and H. Zil of studies on reduced and oxidized glutathione of normal and cataractous lenses and the cystine/cysteine ratio in lens proteins. J. E. Harris and L. B. Gehrsitz reported on the aqueous: plasma steady-state ratios—their variations and significance, and A. deRoetth, Jr., reported on cholinesterase activity in ocular tissue.

The first day's scientific session was followed by a reception and banquet at the Bohemian Club. At the banquet Dr. W. L. Benedict, one of the founders of the association, described the circumstances which led to the founding of the organization.

The second day's session was opened by L. O. Ely with a paper on the oxidation of lactic acid, pyruvic acid, and various members of the citric-acid cycle by bovine lens homogenates.

This was followed by a paper by John E. Harris and L. B. Gehrsitz on the significance of changes in potassium and sodium content of the lens—a mechanism of lenticular intumescence. This important biochemical work would appear to have immediate clinical significance in connection with angle-blockage glaucoma.

The inhibition by thiamine chloride on retinal responses caused by nicotine was discussed by A. I. Fink. Its chief clinical interest lay in the fact that there is a widening of the normal angioscotoma after inhalation of cigarette smoke; thiamine chloride was able to inhibit the alterations of this angioscotoma.

The Proctor Award lecture was given by Phillips Thygeson on the subject of the trachoma, psittacosis, lymphogranuloma venereum group of viruses. The recent work on these viruses has led to their separation into a special group under the family name of Chlamydozoaceae.

J. T. Dameron emphasized to ophthalmologists the advantages of using the anterior chamber of the eye for biologic investigation of problems related to growth and tissue transplantation. He reported a 50-percent to 60-percent take when adrenal, ovarian, testicular, and thyroid embryonic tissues were transplanted to the anterior chamber of the normal adult guinea pig and rabbit. The transplants grew and developed from the fetal form of these glands to the mature form.

A. E. Maumenee reported on the influence of donor-recipient sensitization on corneal grafts and showed that a donor-recipient sensitization can cause a destruction of the stromal cells in the corneal graft with consequent clouding. He pointed out that corneal grafts in rabbits maintain their identity for at least two months after they are inserted.

W. Buschke presented an experimental study on stored corneas, and H. Odenheimer and P. Thygeson reported on the effect of aureomycin, chloromycetin, and terramycin on herpes simplex virus infections in the mouse and rabbit. These antibiotics appear to have only an inhibiting effect on herpes simplex virus and were not truly virividal.

The scientific session was closed with papers by A. N. Barber, R. W. Brauer, R. J. Muelling, Jr., on the effects of beta irradiation applied circumferentially to the ciliary body of rabbits, and by J. M. Dixon and E.

V. Paul on pathologic changes in retrolental fibroplasia.

This was the third two-day meeting of the association and the quality of the papers and interest of the audience were such as to indicate probable continuation of the lengthened session. Dr. James H. Allen was reëlected secretary-treasurer, and Dr. William B. Clark was elected to the board of trustees. Dr. Kenneth C. Swan will be chairman of the 1951 meeting.

The trustees reported an arrangement with the AMERICAN JOURNAL OF OPHTHALMOLOGY according to which the transactions of the association will be published as a thirteenth issue of the JOURNAL. The 1951 meeting is to be held in Philadelphia immediately preceding the American Medical Association convention in Atlantic City.

SECTION ON OPHTHALMOLOGY OF THE AMERICAN MEDICAL ASSOCIATION

The annual three-day session of the Section on Ophthalmology of the American Medical Association was opened with the address of the chairman, Dr. A. Ray Irvine of Beverly Hills, California, who spoke on the progress in ophthalmology in the past 50 years.

Fifteen scientific papers were presented and adequately discussed. They covered a wide variety of clinical and pathologic subjects, varying from the important pathologic study by Parker Heath on primary massive separation of the retina in infants and children to the interesting clinical study by L. V. Johnson and W. A. Nosik on greater superficial petrosal neurectomy for the relief of chronic bullous keratitis. In the latter study the authors were able to diminish the serous component of the tears in cases of chronic bullous keratitis with the result that the tears became hypertonic and reduced corneal edema by removal of fluid.

One of the most interesting papers of the session was a study on ACTH in the treatment of eye diseases by J. A. Olson, E. H. Steffensen, R. R. Margulis, R. W. Smith, and E. L. Whitney of Detroit, in which the authors reported striking temporary results in the treatment of uveitis and many other ocular infections by the use of ACTH and cortisone. Cortisone was also used topically in a series of cases.

Other papers included a study on choked disc and other types of edema of the nervehead by P. J. Leinfelder, a paper on dislocated lens by P. Robb McDonald, and a paper on the clinical application of night-vision tests by W. J. Holmes.

E. Krimsky reported on objective methods in the investigation of strabismus and stressed the importance of his corneal reflex test, and A. Jampolsky reported on retinal correspondence in patients with a small degree of strabismus. The diagnosis of multiple oculomotor paralyses was discussed by W. E. Krewson, III, and W. Stone, Jr., reported on the complications arising in a series of 120 buried implants and of their treatment.

The scientific session was closed by a paper on goniopuncture by H. G. Scheie in which the technique of goniotomy was modified to produce a subconjunctival fistula. Scheie's studies indicated that this fistula remained open in infantile glaucoma but that the cleft invariably closed in adult cases.

Dr. Robert Masters of Indianapolis was elected chairman of the section for 1951, and Dr. Trygve Gundersen was reëlected secretary. In spite of the absence of many well-known faces because of the International Congress in London, the meeting was well attended. The 1951 session will be held in Atlantic City in June.

The section's scientific exhibits were, as usual, of great interest. C. W. Rucker and T. E. Keys exhibited a collection of all the important atlases of ophthalmoscopy which have appeared since the invention of the ophthalmoscope by Helmholtz in 1850. A pamphlet was distributed which gave an annotated description of each atlas. This exhibit was supplemented by one commemorating the Helmholtz centenary on the development of the ophthalmoscope by F. C. Cordes,

M. J. Hogan, and O. H. Ellis. The latter exhibit contained various types of ophthalmoscopes, from an original Helmholtz ophthalmoscope, through the various modifications, and up to and including the recent electrical models. H. F. Falls and F. Bruce Fralick exhibited primary chorioretinal aberrations with night blindness, and D. P. Bell exhibited the pathology and clinical signs of external diseases. G. Floyd and P. C. Kronfeld exhibited individual stereograms of various pathologic fundus conditions taken with a Nordenson camera. The exhibits on the atlases of ophthalmoscopy and the development of the ophthalmoscope received special mention.

Phillips Thygeson.

NEEDLESS REFERRALS

There are few ophthalmologists who have not been consulted by anxious parents with a child whose "vision," they have been told by the school, is defective. If their complaint is not this specific, it may be only that ". . . something is wrong with his eyes." Meanwhile, during the relating of the case history by anxious parents to the interested ophthalmologist, the child in question often stares calmly but perhaps interestedly around the office. When the child himself is asked a direct question, such as "How do your eyes bother you?" his answer will often be ". . . they don't." Somewhat nonplused by this answer, the physician nevertheless proceeds with a complete examination. At its conclusion, he will have found nothing—nothing, that is, but a perfectly normal pair of eyes in an apparently healthy child.

The manner in which the oculist chooses to tell the parents that there is nothing wrong with their child's eyes is particularly important. Consider for a moment who it was in the school that sent the note to the parents that "something is wrong" in the first place. It may have been the teacher or it may have been the school nurse, more likely the latter.

The basis for the note may have been mere observation of the child's behavior, the results of a visual acuity test, or the results of a series of more elaborate tests given on some visual screening device; more and more of the latter are appearing in use in the schools of today.

The important thing is that someone had —or thought they had—a reason for suspecting an ocular defect. The manner in which we tell the parents that there is in fact no defect can affect their subsequent attitude toward not only the school and the school nurse but toward ourselves as oculists.

If the information is given in an abrupt, gruff, "I'm-too-busy-to-be-bothered-with-cases-where-nothing-is-wrong" manner, the reaction of a normal parent is to accept the ophthalmologist's word and then condemn the school nurse or teacher. After a day or two, the experience will often begin to rankle in the mind of the parent and frequently there is a turning against the ophthalmologist too—partly because a fee was charged when nothing was found to be wrong. This is, of course, illogical but is, nevertheless, the way that many persons react. If, at some future date, something is actually found wrong with the child's health during a school examination, a note sent home to the parents is likely to be ignored as "another false alarm."

How much better is the entire situation if the ophthalmologist informs the parents that nothing is wrong in a manner something like this: "You are fortunate in two ways. In the first place, a careful examination has revealed that there is nothing seriously wrong with your child's eyes and that whatever it was that made the school nurse or teacher suspicious must have been temporary. In the second place, you are fortunate to have your child in a school where some attention is paid to more than mere books. The school is apparently interested enough in your child to examine him and, at the time of the examination, his eyes didn't seem to be normal. There are children who are not fortunate enough to be watched that closely in school and occasionally they may have

serious visual defects which remain undetected for years. Such a situation is certainly detrimental to a child and to his school life. Even though this examination has revealed nothing wrong with your child's eyes, you can be grateful and confident that you are not the only one interested in your child. His school is interested too."

The response of the average parents to this type of reasoning is almost invariably good. They no longer will leave the office feeling that this was a needless referral. Not only do they now know what, perhaps, before they had merely taken for granted, that their child's eyes are normal but there is a feeling of confidence and pride in the school system. And this is as it should be.

Ideally, of course, every child would have an ophthalmologic examination prior to beginning school. Practically this is not possible. The next best thing is for the schools to do the best they can with the equipment they have in attempting to detect physical defects and call them to the attention of the parents. Such a program will obviously result in a certain number of needless referrals. The manner in which the ophthalmologist handles the needless referral can make a big difference in the relationships between family and school. It is something worth thinking about.

Richard G. Scobee.

OBITUARIES

HARRY SEARLS GRADLE
(1883-1950)

After an illness of several years, Dr. Harry Searls Gradle died at his home in Sherman Oaks, California, on May 25th, aged 66 years. Dr. Gradle was born in Chicago, December 31, 1883. He attended the University of Michigan, Ann Arbor, where he was graduated from the Department of Liberal Arts with the degree of A.B. in 1906. His medical training was at the Rush Medical College where he earned the degree of M.D. in 1908. During the next two years he pursued graduate medical training in ophthalmology in Vienna, London, Berlin, Paris, and Prague. He was active in the teaching of ophthalmology and was assistant professor of ophthalmology at the University of Illinois College of Medicine from 1921 to 1927, professor in 1944-45, and extramural professor of ophthalmology at Northwestern Medical School from 1928 to 1944.

He was a fellow of the American Medical Association, American College of Surgeons, a member of the American Ophthalmological Society, the Ophthalmological Society of the United Kingdom, Chicago Medical Society, Illinois State Medical Society, American Association for the Advancement of Science, the Association of Military Surgeons of the United States. He was particularly active in the instruction program of the American Academy of Ophthalmology and Otolaryngology. He became a fellow of the Academy in 1911 and served on the Council in 1920 and 1921.

He was instrumental in the establishment of a registry of ophthalmic and otolaryngologic pathology at the Army Medical Museum. In 1921 Dr. Gradle, who served as a first lieutenant in the Medical Corps of the Army of the United States in France, arranged for the establishment of a registry of pathology through the financial support of the academy. The present Registry of Pathology under the auspices of the National Research Council grew out of this sponsorship. In 1921, Dr. Gradle was made chairman of the committee on instruction which is now a major function of the educational program of the academy. He directed the course of instruction until 1938 when he became president of the academy. When the home-study courses were established in 1940, Dr. Gradle was installed as secretary for the home-study courses and directed this activity until 1946 when he retired because of ill health.

In coöperation with Dr. Moacyr Alvaro of São Paulo, Brazil, and Dr. Conrad Berens

of New York, Dr. Gradle organized the first Pan-American Congress of Ophthalmology held in Cleveland in 1940. He was president of the Pan-American Association of Ophthalmology from 1940 to 1946. During the second World War, Dr. Gradle was chairman of the subcommittee on ophthalmology of the National Research Council. He was also chairman of the committee on ophthalmology in the Department of the Interior and worked for the eradication of trachoma among the Indians in the United States.

In 1948 he was awarded the first Pan-American medal of the National Society for the Prevention of Blindness. For many years he was vice-president of the Illinois Society for the Prevention of Blindness and was chairman of the committee on ophthalmology of the Illinois Public Aid Commission Blind Assistance program.

Dr. Gradle was attending ophthalmologist to the Michael Reese Hospital, the Cook County Hospital from 1922 to 1928, and Illinois Eye and Ear Infirmary where he was chief of staff from 1933 to 1945. In 1946 he received the Dana Medal for outstanding service in prevention of blindness. He was on the editorial staff of the AMERICAN JOURNAL OF OPHTHALMOLOGY and of *Ophthalmologia Ibero-Americana*.

Dr. Gradle was a skillful surgeon and maintained a life-long interest in the study of means to improve surgical technique in all forms of intraocular surgery. His interest in glaucoma was manifested by the writing of many papers. He was in great demand as a lecturer before medical societies and was a member of many committees on education and research. He was one of the founders of the Association for Research in Ophthalmology. Dr. Gradle's personal charm made him friends throughout the world in his professional as well as social activities. His contributions to medical science and to the practice of ophthalmology are widely recognized.

William L. Benedict.

HARRY FRIEDENWALD
(1865-1950)

Dr. Harry Friedenwald, son of Aaron and Bertha Stein Friedenwald, was born September 24, 1865, in Baltimore where he resided until his death April 8, 1950. He received his A.B. from the Johns Hopkins University in 1884 and his M.D. degree from the College of Physicians and Surgeons, Baltimore, in 1886. After postgraduate work in Berlin and Vienna, he returned to Baltimore and entered the practice of ophthalmology and otology. He became associated with the College of Physicians and Surgeons where he became the head of the department of ophthalmology in 1902. He continued as head of the department of ophthalmology after the college merged with the University of Maryland until 1929 when he was made emeritus professor.

DR. HARRY FRIEDENWALD

Dr. Friedenwald was a member of the American Ophthalmological Society of which he was president in 1937 and chairman of the Section of Ophthalmology of the

American Medical Association in 1931. He was a member of the Ophthalmological Society of the United Kingdom and many other local and national societies. He was a visiting surgeon to many of the Baltimore hospitals but his chief interest was in the Baltimore Eye and Ear Hospital where he was an active member of the staff and board until his death. In 1930, he gave the Doyne lecture at the Oxford Ophthalmological Congress and, in 1941, the deSchweinitz lecture in Philadelphia.

Dr. Friedenwald made many contributions to ophthalmic and otological literature. The total number of papers relating to ophthalmology was about 115. There were 20 on otological subjects. He also wrote about 50 articles dealing with historical and religious subjects. Notable among his articles upon ophthalmic subjects were those relating to retinal changes, especially those caused by diabetes and vascular lesions.

In addition to his professional interests, he was active in the Zionist movement and was the author of "The Jews in Medicine" and "Jewish Luminarite in Medical History." Through his force of character and high ideals he rendered distinguished service to the institutions he served and the ophthalmic profession in general.

Clyde A. Clapp.

CORRESPONDENCE

Actions of Extraocular Muscles

Editor,
American Journal of Ophthalmology:

In the May, 1950, issue of the American Journal of Ophthalmology the paper by Dr. Anthony Ambrose entitled, "Actions of the extraocular muscles," deals with some interesting problems which, as the author states, have not been adequately dealt with in some textbooks. Dr. Ambrose is to be commended for bringing attention to these problems. However, in his paper some anatomic and mechanical fundamentals have been overlooked with erroneous deductions.

In his paper Dr. Ambrose states, "the superior rectus turns the eye up and out and not up and in;" also, "that the inferior rectus turns the eye down and out and not down and in." These statements require amplification.

Duke-Elder (*Textbook of Ophthalmology*, v. 1, p. 604), Verrijp (Berens, *The Eye and Its Diseases*, p. 850), Scobee (*The Oculorotary Muscles*, pp. 26-28), and others have all called attention to the anatomic fact that, with the eye in the primary position, the muscle plane of either the superior or inferior rectus forms an angle of about 25 degrees with the visual axis. With the eye in this position the line of pull of either muscle is nasal to the center of rotation of the globe; also both muscles are inserted anterior to the center of rotation. Therefore, with the eye in the primary position, any pull that is being exerted by either muscle would have an adducting but no abducting effect. With the globe abducted at an angle of 25 degrees the line of pull of either of these muscles coincides with the visual axis and any pull exerted by either of these muscles would have no abducting or adducting effect, but the effect would be that of elevation or depression only. With the globe abducted beyond this angle, the action of one of these muscles would have some abducting effect but it is doubtful if this is of much practical significance.

These observations focus attention on a somewhat paradoxical condition that exists when a movement is made from the primary to an up and out position (while abduction and elevation are occurring). The superior rectus must, of course, go into action to bring about this elevation. By acting, the superior rectus creates a greater adducting pull than would this muscle when the eye was in the primary position. Or to express it differently, while the superior rectus is exerting a greater adducting pull the globe is being abducted and elevated.

This appears paradoxical and creates a

question as to how this increased adducting pull is nullified. Is it entirely by the lateral rectus? That is extremely doubtful. Sherrington (see Duke-Elder, *Textbook of Ophthalmology*, v. 1, p. 576), has amply shown that the lateral and medial rectus muscles function by the principle of reciprocal innervation in that, when one of these muscles contracts, there is a corresponding relaxation of the other (antagonist) muscle.

It is very likely that this principle functions with regard to the vertically acting extraocular muscles and that the superior and inferior rectus muscles are true antagonists from an innervational viewpoint. Thus, though action by the superior rectus creates a greater adducting pull by this muscle while such a movement is occurring, this is nullified by relaxation of the inferior rectus leaving the abducting portion of such a movement accounted for by the contraction and relaxation of the lateral and medial rectus muscles, respectively.

A similar explanation is applicable for a movement from the primary to a down and out position.

In a paper concerning innervational factors of the vertically acting extraocular muscles to be published in this JOURNAL, reciprocal innervation will be referred to in a more detailed manner.

(Signed) Robert S. Hewitt,
Lincoln Park, Michigan.

CLINICAL OPHTHALMIC TRAINING IN ALASKA

Editor,
American Journal of Ophthalmology:

Following is a letter from Dr. A. W. Vogel, first resident accepted for clinical training in ophthalmology and otolaryngology in Alaska. The Alaska Department of Health is anxious that this important program be continued. Interested physicians should communicate with Dr. Milo H. Fritz, Anchorage, Alaska. A brief résumé of professional experience and the name and address of the chief of the service from which the resident will be released should be included.

(Signed) C. Earl Albrecht, M.D.,
Commissioner of Health,
Juneau, Alaska.

DR. VOGEL'S LETTER

Dear Doctor:

Recently I returned from a six months' tour of EENT practice in Alaska, which was part of my training with Duke University Hospital, approved by both boards, and financed by the Alaska Department of Health. Dr. Milo H. Fritz, of Anchorage, Alaska, who was my preceptor, has recently written a brochure giving the aims of his program, what it has accomplished, and its potentialities. At the risk of some repetition, I am writing to give a first hand account of this medical extension program.

I took the position as the first resident in the program: (1) Because I thought it was a wonderful opportunity to get away from the formality of the "marble and steel halls" of the teaching institutions, and thus do more and see more on my own, and assume more responsibility, yet have expert knowledge to turn to in a time of doubt via radio, telegraph or, if the occasion arose, in person; (2) it promised to show me Alaska, which I had always wanted to see; and (3) but not least, I felt that programs like these are potentially one of the concrete answers which the medical profession can make to socialized medicine.

I realized that I was taking a chance in accepting the position because it had never been tried before. I wish to state that any doubts I had about it were dispelled very shortly after working with Dr. Fritz, and seeing the enormous amount of EENT work that needs to be done in Alaska. I consider the six months I spent in this program in Alaska to have been the most worthwhile

I have spent in my medical training in point of learning to deal with people, using my ingenuity in ticklish medical and diplomatic situations, and in knowing what medical talents I possessed were being used by persons, who, if I did not treat them, would have no EENT care at all.

Literally, I covered all of Alaska—from Sitka to Point Barrow. The equipment is excellent—Poser slitlamp, V. Mueller sharps, Green phoropter, and so forth, and the work in EENT, although not presenting the great variety that one would expect in a teaching center, was excellent for my stage in training. I did about 15 squints, four cataracts, 75 tonsils, two dacryocystorhinostomies, one mastoid (acute), 600 refractions or eye examinations. The next man will get more cataracts at the Pioneers Home in Sitka and more mastoids.

This is not a complete list nor detailed, but will indicate what a man could expect in the way of surgery. As you know, corneal scarring and vascularization from phlyctenular keratoconjunctivitis is the scourge of the territory and beta irradiation will probably be tried on certain of these cases by the next resident, as an Iliff applicator has recently been added to the equipment.

To go into detail about the wonderful scenery, the lovable and gentle Eskimos, the interesting things that I saw while working with the natives and travelling through the country, would take many more pages.

It would be unfair to "sell" this program to a man. He should be willing to put up with minor discomforts such as holding clinics in made-do places—school rooms, barber shops, and so forth—helping four trunks of equipment to and from the bush planes, and the old fashioned plumbing of the smaller villages.

This program is unique, its principles are sound, and the time I spent in Alaska I feel has been invaluable. I envy the next man to take the residency.

(Signed) A. W. Vogel.

BOOK REVIEWS

Estrabismos y Paralisis, Clinica y Terapeutica. By Jorge Malbran. Buenos Aires, Editorial Oftalmologica Argentina, 1949.

This 680-page book deals "in extenso" with the two subjects of strabismus and paralysis of the muscles of the eye, especially from the clinical and therapeutic standpoint. That such a large volume has been devoted to two subjects which in the ordinary textbooks are described in two or three chapters shows how exhaustive the author's studies of the subject have been. Dr. Malbran belongs to the younger generation of Argentine ophthalmologists who have shown such a high level of scientific attainment and vigorously advanced the development of ophthalmology in Latin-America.

The book is well written, the subjects developed scientifically and the clinical descriptions and pathogenesis follow the lead of American and European teachers. It is provided with an extensive bibliography in which the works of Duane, Dunnington, Bielschowsky, Marquez, Guibor, and others are frequently quoted.

In the first chapter, the author studies the anatomy and physiology of the ocular muscles, considering the eye as a mobile body and describing its positions of rest and movement. Then he considers the forces which move the eye, namely, the muscles with their different characteristics, their components, and the causes of impairment of movement. After that he studies the coördinated mechanisms of the eyes and the motor centers in the brain, the muscular tone, and, finally, the muscular associations of the two eyes.

The second chapter deals with the sensory mechanism of binocular vision studying the retinal correspondences, the horopter, and the retinal antagonisms. The third chapter takes up the latent disturbances of muscular equilibrium of the eye closely following the American authors' ideas and also giving

Bielschowsky's studies on the subject an important place. Then Malbran describes the different phorias, the insufficiency and excess of convergence, and gives a complete description of the symptomatology and pathogenesis of these disturbances.

Chapter 4 studies the manifest strabismus and the methods of detecting it and classifying the different clinical types of the disease. Then he studies diplopia in the concomitant and paralytic strabismus. This chapter is illustrated with numerous figures of the varied positions of the eyes.

Chapter 5 considers the vision of strabismic patients, the retinal correspondence and the methods of determining it, the binocular vision, and the visual field in strabismus. Finally Malbran takes up amblyopia ex anopsia or strabismic amblyopia in Chapters 6 and 7.

Chapters 8, 9, 10, and 11 deal with the etiology and pathogenesis of strabismus, the diagnosis, the clinical forms, the prognosis, and optical and surgical treatment.

Chapter 12 takes up the study of paralysis of the eye muscles in general, giving its etiology, classification, and diagnosis. Then, in the following chapters Malbran very thoroughly describes the supranuclear, nuclear, and radicular paralysis and fascicular deviations. Basal paralysis is treated in the 16th chapter and orbital paralysis in the 17th. Chapter 18 covers the diagnosis and treatment of all ocular paralysis.

The book ends with a number of clinical cases which are carefully described and illustrated. The illustrations consist of photographs of the different positions of the eye in the various types of strabismus and paralysis. The author follows the old school of double positions of the observer in regard to the patient. The majority of the pictures show the patient in front of the observer, but for the clinical interpretations sometimes the findings are considered in reference to the physician's own eyes.

Since 1922* I have been emphasizing the importance of reverting in all descriptions of the patient's eyes and their pathologic interpretations to what I called the "Anatomical method," that is, always considering the patient in front of the observer not only for the visible clinical symptoms, but also from the standpoint of the lesions in the orbit, the brain, and so forth. In this way, no strain of the imagination is necessary to visualize the correspondence of the clinical symptoms and ocular deviations and their connection with the central lesions. I have also emphasized the importance of registering the field of vision in the same way, that is, always considering it as projected in front of the patient's eyes and not from the observer's position.

Dr. Malbran's book is to be commended to all ophthalmologists who are especially interested in the pathology of the ocular muscles. It is highly desirable that an English translation be made available for English-speaking ophthalmologists.

M. Uribe Troncoso.

LES UVÉITES HYPERTENSIVES. By Marcel Kalt. Paris, Masson et Cie., 1949. Paper binding, 406 pages, 64 figures, and 8 pages of colored plates. Price: 2,000 francs.

Kalt distinguishes three types of uveitis with increased intraocular pressure: (1) "True hypertensive uveitis" with primary cyclitis and concomitant increased tension; (2) glaucoma secondary to cicatricial sequelae of iridocyclitis; and (3) "pseudo hypertensive uveitis" in which a uveitis complicates preëxisting glaucoma. Among special varieties of true hypertensive uveitis are serous cyclitis and menopausal cyclitis. In the former, although the eye is white and the pupil round, slightly dilated, and free from synechias, biomicroscopy discloses the characteristic whitish keratic precipitates, dustiness of the anterior vitreous, and perhaps the nodules of Schieck. Menopausal cyclitis

* M. Uribe Troncoso: Ophthalmological versus anatomic nomenclature. Proceedings of the International Congress on Ophthalomology, Washington, 1922.

is an insidious grave form that is often bilateral.

Kalt agrees with Morax that pilocarpine acts favorably in acute serous cyclitis without synechias, but in subacute forms its use is dangerous. In general, adrenalin (two percent) is the agent of choice. The effect of adrenalin decreases with the duration of the disease. Atropine lowers the tension in two thirds of cases but is likewise less effectual in the chronic forms. Pilocarpine is then often helpful but must be alternated with the secondary mydriatics (homatropine, one percent; ephedrine, four percent) to avoid synechias. Retrobulbar injection of alcohol (40 to 50 percent) adequately relieves pain, but lowers the tension in only one fifth of the patients.

In uveitis the eye is more tolerant to increased tension than in primary congestive glaucoma, but an early contraction of the field, most often nasally, is characteristic. Kalt consequently advises surgery when a tension above 40 mm. Hg persists over two weeks. The reaction of paracentesis is variable, but seems more constantly favorable in the cicatricial type. Weekers, whom Kalt cites at length, considers paracentesis useless, except when done after his nonperforating, "indirect" cyclodiathermy, to counteract the immediate postoperative rise of tension. In this procedure, which Kalt favors as a last resort in acute cases, the diathermy is done at the level of the ora serrata, eight mm. from the limbus, where terminal ramifications of the long and short ciliary nerves arborize with sympathetic ganglion cells to produce a supraciliary plexus. An intense vasodilatation is induced which generates hypotension. With the pyrometric technique and minute electrodes (0.75-mm. diameter), 12 to 20 applications can be applied transconjunctivally along the circumference. In subacute or chronic cases, however, Kalt prefers iridencleisis ab externo as the procedure of election.

This valuable monograph includes a comprehensive and critical analysis of previous work, a discussion of all experimental methods of investigation, Kalt's personal studies in detail, and a most complete bibliography.

James E. Lebensohn.

TRANSACTIONS OF THE SOCIÉTÉ FRANÇAISE D'OPHTHALMOLOGIE, 1949, volume 62, pp. 1-476

These transactions of the French Society of Ophthalmology contain reports on the meetings of May 22 to May 26, 1949. It is a masterly book which only could be achieved by authors who have had intensive personal experience with an extensive clinical material and research work, combined with thoughtful consideration and conservative judgement, as well as a good knowledge of a voluminous literature.

"Hypertensive uveitis," presented by Marcel Kalt and since published in monograph form (reviewed in this issue of the JOURNAL by Dr. James E. Lebensohn) was the main topic of discussion. The author was congratulated by all discussers because of his superior handling of this difficult and controversial subject and because of the completeness of his review.

François points out that gonioscopy is of little help in the explanation of hypertension in iridocyclitis. Since the chamber angle is not the only place for the resorption of the aqueous, the tension can be normal when it is blocked and increased when it is open. Attention is drawn to the elimination of aqueous through the vitreous and the iris veins. Atropine in normal eyes increases the width of the chamber angle by a posterior retraction of the ciliary processes, it does not block the angle in hypertensive uveitis, but it does so in some narrow-angle glaucomas either because of a protrusion of the lens or a structural variation of the iris root.

The passage of fluorescein and the difference in the elmination curve in acute hyper-

tensive and chronic uveitis was interpreted by several authors. Goldman described a new method of fluorometry and Verrey discussed his very interesting analysis of the chemistry, cytology, and bacteriology of the aqueous.

Bailliart still seems to think that syphilis is the main cause of uveitis, while J. Sedan stresses the possibility of a tuberculous origin and Nectoux of focal infection. In the treatment of hypertensive uveitis, Kalt does not use vasodilators but favors the use of any drug that decreases the permeability of the capillary wall and increases the blood-aqueous barrier, such as vitamin P, rutin, and 20-percent calcium gluconate. Surgery was only recommended after failure of drug therapy.

Fifty-five papers on various subjects were read during the four-day session, most of them of more than average interest. Martin-Amat calls attention to a localized anesthesia of the cornea as a sign of intraocular growth. Valiere-Vialeix studied the chemical, histologic, and especially biomicroscopic changes in a fluid vitreous after a total collapse of the eyeball due to severe vitreous loss during cataract extraction.

L. Paufique recommends lamellar keratoplasty as the most successful therapy in severe insidious chronic and recurrent keratitis of various origins. The corneal material is taken from cadavers and prepared for five days in the refrigerator at a temperature of 4°C. Corneas which have already been partially used for optical keratoplasty may be used again after having been replaced into the solution and the freezing chamber for several days.

C. Bonamour states that retinal hemorrhages in the newborn have a good prognosis, and that they are not the cause of unexplained macular lesions, amblyopias, and squints.

There exists a hypertension in youth which must be differentiated from congenital glaucoma, the chronic glaucoma of the adult, the familial hereditary glaucoma, and secondary glaucoma. Jean Gallois calls it preglaucoma. Its only symptoms are headaches; its only signs, increased tension; and its control, by pilocarpine. The provocation tests are negative.

Alice R. Deutsch.

HANDBOOK OF PHYSICAL MEDICINE AND REHABILITATION. An official A.M.A. publication by 29 authors. Philadelphia. The Blakiston Co., 1950. 573 pages, illustrated, with index. Price, $4.25.

This publication, sponsored by the Council of Physical Medicine and Rehabilitation of the American Medical Association, includes 30 chapters by diverse authors. The special chapter in reference to ophthalmology consists of 29 pages and is contributed by Ray K. Daily and Louis Daily, Jr., who have given an over-all picture of the applications of physical medicine to ophthalmology. Adding to the value of their text is a quite complete bibliography of 136 references. They conclude that physical therapy is a useful addition to the therapeutic armamentarium of the ophthalmologist, though not a substitute for otherwise effective therapy.

James E. Lebensohn.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned in one only. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Sondermann, R. **The development of the corneal endothelium.** Arch. f. Ophth. **149**:690-694, 1949.

Histologic examination of human embryos makes it probable that the corneal endothelium develops from corneal and lenticular epithelial cells and is, therefore, not a true endothelium. Ernst Schmerl.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Amsler, M., and Huber, A. **The blood aqueous barrier, its clinical meaning.** Arch. f. Ophth. **149**:578-585, 1949.

A short summary is presented of formerly published studies in which intravenous injections of 2 cc. of a 10 percent fluorescein-sodium solution were used and the appearance of the fluorescein in the anterior chamber was studied.

Ernst Schmerl.

Bietti, G., and Scano, A. **The pupil in anoxia.** Atti d. 37 Congresso Soc. ital. oftal. **10**:58-59, 1948.

The most interesting result in these pupillographic studies was the constant mydriasis in anoxia which the authors believe to be due to an increased adrenalin level in the blood. Frederick C. Blodi.

Campbell, F. W., and Whiteside, T. C. D. **Induced pupillary oscillations.** Brit. J. Ophth. **34**:180-192, March, 1950.

If a slitlamp is adjusted so that the vertical image of the slit falls on the edge of the iris and just overflows through the pupil to fall on the retina, the pupil will contract and then, having contracted, the iris cuts the beam of light off the retina and the pupil enlarges again. There are definite latent periods between each phase and this allows good and easy observations of these continuous oscillations of the iris. These observations were carried out on a Gullstrand clinical slitlamp and two stop watches calibrated in fifths of a second and film recordings were made by means of ultraviolet light.

The oscillations were more regular with the beam of light just at the pupillary edge rather than nearer the pupil center. Fatigue of the iris seemed to play no part up to 200 continuous oscillations. Previous dark adaptation caused an increase in the rate of hippus for the first five minutes and previous light adaptation caused a decrease in the rate for the first

five minutes after which the rate returned to normal. The size of the pupil seemed to have the greatest bearing on the hippus rate. The frequency was higher with a smaller pupil and lower with a larger pupil. Morris Kaplan.

Capolongo, G. **Lactoflavin [riboflavin] in the metabolism of the retina.** Ann. di ottal. e clin ocul. **75**:271-278, Sept., 1949.

Recent views on the presence of riboflavin in the eye, its significance and its probable action, are briefly discussed. Using Warburg's manometric method, Capolongo studied the respiration and the aerobic and anaerobic glycolysis of the retina of normal rats and of rats deprived of riboflavin, and confirms the concept that riboflavin in the retina of mammals also plays a role in oxidation-reduction processes.

Harry K. Messenger.

Chait, R. A. **Absorption of protein through the conjunctival mucous membrane.** Arch. Ophth. **43**:526-528, March, 1950.

The absorption of protein through the conjunctival mucosa has not been reported. It was the purpose of this study to demonstrate, by immunologic means, that unaltered protein may be absorbed through the conjunctival mucous membrane of the human eye. Walzer and his associates have shown that a cutaneous site which has been sensitized to an allergen will react after the systemic absorption of that allergen through various portals of entry.

A negro girl, 6 years of age, who at the age of two years had undergone extirpation of her lacrimal sacs for chronic dacryocystitis, was the subject of this experiment. Twenty-one minutes after the introduction of the allergen into the conjunctival sac a reaction appeared at the sensitized cutaneous site. Intense pruritus was rapidly followed by marked erythema and a large wheal, 7 cm. in diameter. This cutaneous reaction demonstrated the passage of the peanut allergen through the conjunctival mucous membrane into the circulation. R. W. Danielson.

Cristini, G. **The vascular action of pilocarpin, eserin, adrenalin, and atropin and their influence on primary glaucoma.** Atti d. 37 Congresso Soc. ital. oftal. **10**:98, 1948.

Biomicroscopic studies on experimental animals show that atropin dilates the large vessels and increases the intraocular pressure. Eserin and pilocarpin by dilating the capillaries, and adrenalin which dilates all vessels, reduce the intraocular pressure. Frederick C. Blodi.

Dubois-Poulsen, A., Leroy, J., and Couzi, J. **Newer ideas concerning the physiologic ocular action of acetylcholine.** Ann. d'ocul., **183**:265-296, April, 1950.

The ocular effects of acetylcholine administered extra-ocularly as in the shock treatment of maniac-depressive insanity, schizophrenia and other mental conditions are analyzed and discussed in detail. After small doses of 10 to 20 cgm. of the chlorohydrate administered intramuscularly or subcutaneously low arterial retinal and venous pressure follows, usually with myosis and retinal vascular enlargement lasting 5 to 30 minutes. Paradoxically, there is decrease of the blind spot and also a decrease of vascular shadows angioscopically. Ten illustrative cases are presented. Large doses of 40 to 50 cgm. rapidly administered as in shock therapy, produce effects that are quite different. Prompt unconsciousness lasting 30 to 40 seconds with cardiac arrest of approximately 90 seconds, and epileptiform convulsions follow. The ocular symptoms include mydriasis followed by myosis, marked contraction of the retinal vessels followed by dilatation, and occasionally increased ocular tension. Sixteen cases are discussed in detail. The chloro-manganate was found to be most effective. The differ-

ence between the effects of small and large doses is explained by the different effect which acetylcholine has on the peripheral and central nervous systems. Peripherally, acetylcholine is a parasympathetic-mimetic drug, as evidenced in its local use in glaucoma. Centrally, however, it has an adrenergic action. In the large doses used rapidly in shock therapy the central effect overpowers the peripheral action. Chas. A. Bahn.

Dyson, Charles. **Influence of iontophoresis on the permeability of the excised cornea.** Arch. Ophth. **42**:416-421, Oct., 1949.

The epithelium of the cornea not only is virtually impermeable to electrolytes but also possesses a high degree of electrical resistance. Experimental work on excised bovine corneas demonstrates that the resistence of the epithelium to permeation is impaired by the iontophoretic procedure. This change in permeability does not appear to depend on the changes in the hydrogen ion concentration in the buffered solutions employed. The impairment of the barrier would seem not only to permit the ions to move by diffusional processes due to their kinetic energy but, in the presence of continued iontophoresis, to enable them to cross, at an accelerated pace, a previously nonconducting barrier. The appearance of epithelial haze after the use of iontophoresis has been repeatedly observed. It has been suspected that the reported efficacy of iontophoresis may be due to epithelial injury. The reported experimental work confirms this suspicion. John C. Long.

D'Ermo, F. **Effect of paraminobenzoic acid (vitamin H_1) on the healing of experimental corneal wounds.** Boll. d'ocul. **28**:677-688, Nov., 1949.

Chemically known since 1860, paraminobenzoic acid (PABA) was not recognized to be an important factor of the B vitamin group until 1940 when Green, Woods and Kuhn found it to be active in dilution of 1.6×10^{-10} gram per cc. Benda and Poirot (1946) suggested that some of the therapeutic effects of chemically similar novocaine might be explained by this structural relationship. A great number of therapeutic effects have been ascribed to paraminobenzoic acid. Celotti used it successfully in retinal vein thrombosis after the effect of novocaine in thrombosis had been reported. Improved wound healing has been observed in the skin of experimental animals and of man but no studies of corneal wounds had been reported. The author made sterile corneal wounds 3 mm. long, perpendicular to the corneal surface and penetrating the whole thickness of the membrane, in each eye of 20 rabbits. One eye of each of ten animals was then treated with a 10-percent paraminobenzoic acid ointment, the other eye with atropine and penicillin. The remaining ten animals received intravenous and intramuscular injections of paraminobenzoic acid. The rabbits were killed, 2, 4, 7, 9 and 13 days postoperatively and the corneas were examined after staining with hematoxylin and eosin. Locally applied paraminobenzoic acid enhanced the wound healing definitely; the scar formation occurred more rapidly and more regularly than in the corneas treated with penicillin; parenteral application proved less effective. (10 figures, 11 references.)

K. W. Ascher.

Gettes, B. C. **Dibutoline sulfate: comparative clinical study of cycloplegic effects.** Arch. Ophth. **43**:446-453, March, 1950.

Dibutoline sulfate is chemically related to carbachol but possesses mydriatic and cycloplegic properties. It probably produces paresis of the iris sphincter and ciliary muscles by direct action on the muscle cells. No incidence of sensitivity to dibutoline was observed in almost 1,000

eyes. When used alone 5-percent dibutoline offers no advantage over 4-percent homatropine, 1-percent paredrine or 4-percent homatropine alone but dibutoline and homatropine are definitely synergistic. They are an excellent routine cycloplegic; recovery of accommodation after their use is complete within 48 hours.

E. J. Swets.

Giardini, A. **Influence of high altitudes on the visual apparatus.** Boll. d'ocul. **28**: 649-676, Nov., 1949.

The effect of acute and of chronic oxygen deficiency on the eye is discussed. The author evaluates his own observations and those published by others. Six pages of bibliography witness the enormous material that has been integrated. Changes in sensitivity and visual acuity, in the visual fields, in stereopsis, in light perception, differentiability, afterimages, color sense, critical fusion frequency, retinal circulation, intraocular pressure, position and motility of the bulbus, accommodation and convergence, oculomotor equilibrium, fusion and coördinated eye movements are reviewed.

K. W. Ascher.

Hollwich, Fritz. **The influence of the hypothalamic nerve fibers of the optic tracts on functional processes, especially water metabolism.** Arch. f. Ophth. **149**: 592-619, 1949.

The role of the pituitary in water metabolism is known. It could be expected that defects in the innervation of the organ would interfere with the normal water excretion. Part of this innervation comes from the optic tracts through the nucleus supraopticus. In this study the water excretion in 20 blind people is compared with that of 20 healthy subjects. The author uses Volhard's water test and finds that normal as well as blind people show a maximum of excretion during daytime. However, blind persons show a second maximum at night. It might be assumed that in the blind the amount of the circulating antidiuretic principle during the night hours is smaller than in the normal person. Ernst Schmerl.

Jackson, C. R. S. **The action of eserine upon the eye following the use of atropine.** Brit. J. Ophth. **34**:156-160. March, 1950.

Atropine reduces the sensitivity of the muscle fibers to the presence of acetylcholine so that dilation of the pupil results from the tonic pull of the dilator fibers. Eserine has no direct action on nerve endings but acts solely as an anticholinesterase. It allows the concentration of acetyl-choline to rise and so augments the response of the tissue to its nerve.

One of the earliest writers on the subject was Argyll Robertson who found that eserine was quite effective following atropinization. During studies on rabbits it was found that miosis with eserine occurred easily after full and complete atropinization. In addition, six patients are described in whom the effect was equally definite. Morris Kaplan.

Kedvessy, G., de Grósz, S., and Szepesy, A. **Preparation of ophthalmic solutions: modern concepts. 1. Atropine sulphate.** Brit. J. Ophth. **34**:228-234, April, 1950.

The authors completely review the literature. The results of their experimental work show the measure of the physiologic activity of atropine. Isotonic atropine sulphate solution produced no irritation regardless of its pH, but simple aqueous atropine solution caused severe burning. The mydriatic effect increased only slightly with increase of pH. There was no difference between the activity of the atropine base or ion. The decomposition of atropine in simple aqueous solution and in the higher pHs was considerable. The solution recommended should have a

pH of 7 prepared with a boric acid-sodium borate buffer. For preservative zephiran 1:20,000 was recommended.

Orwyn H. Ellis.

Di Luca, Giuseppe. **The ophthalmotonus and its relations to the general and retinal arterial pressure, to the intraocular circulation and to intracranial pressure.** Riv. oto-neuro-oftal. **25**:19-48, Jan.-Feb., 1950.

For the study of the mechanisms regulating the ophthalmotonus, experiments were made on cats, dogs, and rabbits by stimuli of different kind, intensity and duration which can be grouped in three types: pharmacodynamic, nervous (stimulation or resection of the neurovegetative or sensory nerves), and biophysical (variations of carotid and intracranial pressure). It was found that the normal eye possesses a particular mechanism to regulate the ophthalmotonus located in the peripheral circulation of the uvea which is independent from the general circulation and from the blood pressure of the ocular vessels at their entrance into the globe. The vascular factors of the ophthalmotonic equilibrium are mainly the pressure condition of the precapillary arterioles and the capillary network of the uveal tract, and the speed of the circulation. Every other intraocular phenomenon related to the ocular pressure is to be considered as secondary to the variations of these factors. (3 figures.)

Melchior Lombardo.

Macaskill, J., and Weatherall, M. **Streptomycin and promanide in experimental ocular tuberculosis.** Brit. J. Ophth. **34**:147-155, March, 1950.

A human strain of bacteria suspended in 0.9-percent sodium chloride solution was inoculated into the anterior chamber. Two sets of experiments were done. In the first, animals with very severe tuberculous lesions were given subconjunctival injections of 30 mg. of streptomycin in 0.3 cc. sterile 0.9-percent sodium chloride solution once daily for 17 days. No benefit whatever was observed either clinically or histologically and the rate of progress of all the lesions was apparently unaffected.

In the second series the lesions, though similarly induced, were much milder and slower to develop. After onset of symptoms these rabbits were divided, into 4 groups: one had no treatment; one received promanide intravenously every 12 hours; one received streptomycin intravenously at 12 hour intervals and one received both promanide and streptomycin. Improvement was significant only in the streptomycin group.

Morris Kaplan.

Malatesta, C. **Chromatographic determination of keto-acids of the human and animal vitreous.** Boll. d'ocul. **28**:727-732, Dec., 1949.

The vitreous body of man, ox, and rat contains chromatographically determinable amounts of alpha-keto-glutaric and pyruvic acid in roughly similar concentrations. The pyruvic acid concentration is somewhat higher; a third keto-acid was demonstrated but not identified.

K. W. Ascher.

Moro, F. **Benzopyrene injected into the anterior chamber and into the vitreous of rats.** Atti d. 37 Congresso Soc. ital. oftal. **10**:173-189, 1948.

Injection of benzopyrene into the anterior chamber produces a violent inflammation with cataract formation. Injection into the vitreous produces a severe exudative uveitis with circumscribed benign proliferation of the ganglion-cell layer of the retina. Injection into the connective tissue of the orbit precipitates a typical sarcoma.

Frederick C. Blodi.

Swan, K. C. **Ocular effects of the choline esters.** Arch. Ophth. **42**:709-725, Dec., 1949.

A comprehensive discussion of the chemistry and pharmacologic action on the eye of a number of choline esters is presented. The pharmacologic action of these esters seems related to their surface activity. The miotic and cyclotonic drugs are all relatively surface-inactive, whereas the highly surface-active esters of choline have mydriatic and cycloplegic properties. The action and use of a series of synthetic choline derivatives are discussed. These include methacholine chloride (mecholyl), carbochol (carcholin or doryl), and urecholine. A large series of surface active choline esters was synthesized. Dibutoline sulfate is the most effective of these new compounds. It induces mydriasis by inhibition of the iris sphincter and recession of the near point of accommodation. The smooth muscles of the lids and the dilators of the iris, innervated by the sympathetic nervous system, are unaffected. The intraocular effects of dibutoline, therefore, simulate paralysis of the oculomotor nerve and are the reverse of those of acetylcholine. Dibutoline, in the intensity of its mydriatic and cycloplegic action, is comparable to homatropine, but it is less consistently absorbed into the cornea. It has the advantage that the visual disability which it causes is not so prolonged as that of homatropine. It is of value in the management of corneal inflammations because it has detergent and antiseptic actions in addition to its mydriatic and cycloplegic effects.

John C. Long.

Weinstein, Paul. **New concepts regarding anterior drainage of the eye.** Brit. J. Ophth. **34**:161-168, March, 1950.

The author believes that there is a secondary drainage system from the anterior chamber in addition to Schlemm's canal and that this system is a network of aqueous veins which drain away aqueous as well as blood and empty into the jugular system. Probably these two systems are in close communication since pressure upon the jugular produces the retrograde entrance of blood into these aqueous veins. At the same time Schlemm's canal is also seen to fill with blood if the angle is examined gonioscopically. These veins appear at the limbus as laminary vessels and are probably continuations of the thin veins of the ciliary plexus. (11 figures.)

Morris Kaplan.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Auerswald, W., Bornschein, H., and Zwiauer, A. **Biostatistical evaluation of various factors in scotopic vision.** Arch. f. Ophth. **149**:686-689, 1949.

Mathematical considerations deal with the correlation of the various factors involved in scotopic vision.

Ernst Schmerl.

Bailliart, P. **The yellow spot and its pigment.** Atti 37 Congresso Soc. oftal. ital. **10**:47-52, 1948.

A new theory on the physiologic importance of the macular pigment is offered. The retina, as a living tissue, has not an ideal optical homogeneity. The retinal cells have a slightly different refractive index compared with the intercellular spaces. These cells deviate the light and become secondary centers of light emission. This diffraction is highest for the short waves.

The degree of diffraction within the retina depends on the thickness of the tissue and is therefore smallest in the foveola. In the thicker parts of the macula the yellow pigment, absorbing the shorter waves, prevents the intraretinal diffraction and is therefore of great value.

The macular pigment disintegrates with age and this may be one of the causes of senile macular degeneration. The increased absorption of the shorter waves by the lens neutralizes any color effects. But after cataract extraction the blue color may predominate as the macular pigment can not absorb it any more.

Frederick C. Blodi.

Carra, G. **Periodic transient myopia connected with conjunctival congestion, probably allergic.** Boll. d'ocul. **28**:747-754, Dec., 1949.

A 29-year-old healthy soldier had transient attacks of blurred vision occurring in one eye or the other at irregular intervals and accompanied by conjunctivitis. For about 10 days the affected eye revealed myopia of 2 diopters while the other one retained its emmetropic refraction until it, in turn, became transiently myopic. General and ophthalmologic examinations revealed no abnormality except mild eosinophilia. Allergic etiology was assumed. (66 references.) K. W. Ascher.

Chacko, L. W. **Relation of color sensitivity in the visual field to the laminar pattern in the lateral geniculate body.** Arch. Ophth. **42**:402-409, Oct., 1949.

Through indirect evidence, it is presumed that the laminar pattern in the lateral geniculate body of the primates has a specific relation to color vision. If it is assumed that in the projection zone for central vision of the geniculate body the large cell layers for each eye subserve the blue region of the spectrum, the dorsally situated laminas, in which smaller cells are in the majority, may mediate impulses elicited by the longer wave lengths and the intermediate laminas may mediate impulses from the middle portion of the spectrum. Additional directions of investigation are suggested.

John C. Long.

Corrado, M. **Changes in refraction after excision of the stellate ganglion.** Atti d. 37 Congresso Soc. ital. oftal. **10**:92-97, 1948.

Pursuing his studies on the double innervation of the ciliary muscle, the refractivity of an eye was measured by retinoscopy before and after the operation. In two patients so examined the existing hypermetropia decreased considerably. This result corresponds to the increased hypermetropia after stimulation of the sympathetic nerve found by several authors. After excluding other possible explanations the author believes that this can only be explained by assuming that there is also a sympathetic innervation of the ciliary muscle. Frederick C. Blodi.

Glees, M. **The role of depth perception in scotopic vision.** Arch. f. Ophth. **149**:680-685, 1949.

After the loss of one eye people often complain that they do not feel safe, especially in the dark. An examination usually reveals normal dark adaptation. However, the depth perception of a monocular subject is markedly disturbed. The author found this to be true of 80 normal persons under normal and decreased lighting conditions. He obtained similar results in five patients with brain injuries. Their dark adaptation was normal, their fusion seemed to be diminished. Central changes are considered the primary causes of the visual disturbances in people with brain injuries. Ernst Schmerl.

Grimm, R. **The stereoscopic space.** Arch. f. Ophth. **150**:135-143, 1950.

The author discusses the older theories of stereoscopic vision. He considers the stimulation of disparate retinal areas as a functional entity and the binocular depth perception as their function.

Ernst Schmerl.

Hamburger, F. A. **Binocular vision in the cross-eyed.** Arch. f. Ophth. **150**:157-164, 1950.

Thirteen cases are described with retinal inhibition or anomalous retinal correspondence of the squinting eye.

Ernst Schmerl.

Hruby, K. **Corneal astigmatism, astigmatism of the lens and the total astigmatism of the eye.** Arch. f. Ophth. **150**:91-119, 1950.

The author studied several hundred eyes with Javal's ophthalmometer and Lindner's cylinder-sciascopy. He found that the total astigmatism can be considered as the sum of the astigmatism of the anterior corneal surface and the astigmatism of the lens. Roughly the lenticular astigmatism is one and one half times the difference between total and corneal astigmatism. Lens astigmatism occurs rather frequently and often diminishes the total astigmatism. Usually lens astigmatism is of a low or moderate degree. The principal meridians of the corneal and the lenticular astigmatism often do not coincide. A simple correlation between corneal and lenticular astigmatism cannot be recognized.

Ernst Schmerl.

Jäger, A. **Ocular distortion and position of the nodal point.** Arch. f. Ophth. **150**:178-181, 1950.

A mathematical procedure is described which enables the author to express the degree of distortion in angular magnitudes. Ernst Schmerl.

Littmann, H. **Foveal precision skiascopy.** Arch. f. Ophth. **149**:520-539, 1949.

Procedures and instruments are described which enable the research worker to determine refractions skiascopically with an error of ±0.05D.

Ernst Schmerl.

Lo Cascio, G., and de Leonibus. F. **The curvature of the posterior corneal surface.** Atti. d. 37 Congresso Soc. ital. oftal. **10**: 144-147, 1948.

The curvature was measured by the trigonometric method of Nordenson, modified by Berg. The posterior corneal surface has practically no astigmatism in emmetropic eyes. In astigmatism of the anterior corneal surface the posterior surface usually shows a similar deformation which partially neutralizes the total astigmatism. Frederick C. Blodi.

Marquez, M. **The Cajal theory of chiasmal crossing in the cyclopic and "doubled" eye.** Ann. d'ocul. **183**:326-337, April, 1950.

The author discusses the theory of Cajal and graphically illustrates the evolution of the simpler and more complex forms of sight with ten figures.

Chas. A. Bahn.

Meyer-Schwickerath, G. **The role of the environment in myopia. A statistical study of twins.** Arch. f. Ophth. **149**:695-700, 1949.

The author reports two cases of his own and 14 that have been reported. Major differences in degree of myopia are rather common among identical twins and occur in the two twins as well as between the two eyes of one of them. The differences in refraction in a group of myopic twins might be 20 times as great as those in emmetropic twins. This favors the view that higher degrees of myopia must be considered pathologic. Ernst Schmerl.

Nizetic, B., Jr. **The influence of anoxia on the migration of retinal pigment.** Atti d. 37 Congresso Soc. ital. oftal. **10**:209-210, 1948.

In order to shed some light on the decreased light sensitivity of the retina during anoxia the following experiments were

performed. Frogs were kept under low oxygen tension, some were kept in darkness, and some were exposed to light. The frogs kept in darkness and under anoxia showed a position of their retinal pigment similar to the animals exposed to light. This is explained by a hyperadrenalinemia during anoxia and may be one factor responsible for the decreased sensitivity to light. Frederick C. Blodi.

Nordenson, J. W. **Vogt's proofs of the presence of a yellow pigment in the macula.** Arch. f. Ophth. **149**:540-544, 1949.

In red-free light the author finds that not only the macula but also the periphery of the fundus is yellowish. On the other hand and on the basis of certain experiments, he reaches the conclusion that a yellow color of the superficial retinal layers need not necessarily become visible in red-free light. Ernst Schmerl.

Pascal, J. I. **The cardinal points in corrected ametropia.** Brit. J. Ophth. **34**:261-264, April, 1950.

The author diagrammatically represents the cardinal points of the eye as a horizontally placed benzene ring. The displacement of the secondary axis and the increase or decrease of the size of the retinal image can be read directly from the scheme and more easily remembered. Orwyn H. Ellis.

Pau, Hans. **The colloid osmotic pressure of the lens proteins. Their role in accommodative changes of the lens.** Arch. f. Ophth. **149**:701-705, 1949.

Calculations lead the author to conclude that the colloid osmotic pressure of the lens proteins plays a major role in extracapsular mechanism of accommodation. Ernst Schmerl.

Remky, Hans. **Reciprocal induction of the retina as the basic factor of binocular vision.** Arch. f. Ophth. **150**:120-134, 1950.

The author feels that the anomalous retinal correspondence in cross-eyed subjects represents a sensory adaptation of the deviating eye. In this way utilization of the stimuli by the squinting eye is said to be facilitated. Ernst Schmerl.

Rössler, F. **The accommodation of the eye in its relation to the state of the nervous system.** Arch. f. Ophth. **150**:75-90, 1950.

The author studied by his own method the accommodation of the eye with the help of a cobalt filter. Voluntary as well as involuntary factors are involved in the mechanism of accommodation. Ernst Schmerl.

Rubino, A., and Pereyra, L. **The eye and the diencephalon.** Riv. oto-neuro-oftal. **25**:12-15, Jan.-Feb., 1950.

The behavior of the day-night rhythm in the light sense of eight patients with pigmentary degeneration of the retina was about the same as in normal persons. This result confirms the previous statement of the writers that the daily variations of light sense are determined centrally and not peripherally. Melchior Lombardo.

Rubino, A., and Sapuppo, C. **The eye and the diencephalon.** Riv. oto-neuro-oftal. **25**:16-18, Jan.-Feb., 1950.

The reflex light sense in patients with not much advanced forms of retinitis pigmentosa and with vision not lower than 7/10 differed little from that of normal subjects. These findings support the belief of the authors that there is central control of the adaptation of the retina. Melchior Lombardo.

Slataper, F. J. **Age norms of refraction and vision.** Arch. Ophth. **43**:466-481, March, 1950.

Observations made in 35,570 cycloplegic refractions form the basis for this statisti-

cal treatise the purpose of which is to provide the ophthalmologist with knowledge of the average normal vision and spherical equivalent refraction in age groups from birth to 87 years of age. The refraction of the newborn is near plus 2.32 D. The eye becomes more hypermetropic until 7 years of age and gains plus 1.617 D. during this period. During the period from 7 to 30 years of age the eye becomes gradually more myopic and loses 3.327 D. The hypermetropic change of middle age (31 to 64 years) adds plus 1.362 D. From 65 to 87 years of age senile lens changes cause an increase in the myopia of 2.367 D. The average adult refraction in atropine cycloplegia is near plus 1.25 D. The cylindrical error is inconstant in its annual variation but age changes the axis of the cylinder in a definite pattern.

E. J. Swets.

Stanworth, A., and Naylor, E. J. **The polarization optics of the isolated cornea.** Brit. J. Ophth. **34**:201-211, April, 1950.

The authors describe an apparatus for investigating the isolated cornea in polarized light under conditions as close to physiological as possible. The isogyres are almost identical in man, dog, cat and rabbit. Light in the pupillary area of the cornea shows extremely small birefringence, but the latter increases as the periphery is approached. The interference figure is thought to be the effect of the oblique incidence of the ray of light falling on the anisotropic corneal lamellae. The arrangement of the corneal lamellae and the stresses of the cornea may be secondary factors. The interference figure is not changed by an elevation of the pressure behind the excised cornea. It is proposed to study the effect of light passing obliquely through the cornea in an effort to obtain the bi-refringence of lamellae running only in one direction.

Orwyn H. Ellis.

Thomson, L. C. **The nervous system in visual adaptation.** Brit. J. Ophth. **34**:129-146, March, 1950.

At night the eye may be as much as 10,000 times more sensitive to light than it is during the day. Most students believe that this is entirely a photochemical phenomenon, brought about by the bleaching and regeneration of light sensitive pigments. Others maintain that in addition to the photochemical changes there are changes in the sensitivity of the nervous apparatus as well. The photochemical theory was propounded by Hecht who does not admit of any change in the sensitivity of the nervous system during the process. It is pointed out however that there is a large discrepancy between the magnitude of the change in concentration of photosensitive material and the change in the sensitivity of the visual mechanism. The accumulation of visual purple is approximately doubled when the sensitivity to light of the dark-adapted eye is increased 1000 times. This very definitely indicates the existence of some other factor, which most probably is an increase in nervous sensitivity. Furthermore, a bilateral increase of sensitivity when only one eye is withdrawn from illumination points very strongly to an increased sensitivity of the nervous elements.

Morris Kaplan.

Weale, R. **After-images.** Brit. J. Ophth. **34**:190-192, March, 1950.

In 1945 Edridge-Green reported experiments which indicated that the rods are not percipient elements but gland-like structures secreting visual purple; that the cones are not stimulated directly by light but indirectly by the decomposition products of visual purple; that visual purple is secreted into a space filled with fluid in which the tips of the cones are immersed; that under certain circumstances relative movement can take place

between this fluid and the tips of the cones. With some of these conclusions the author disagrees. In a series of experiments the details of which are described, it was ascertained that different results were obtainable if foveal or extrafoveal vision was used; that in foveal vision the above held true, but that in extrafoveal vision variations occurred especially as regards the effect of movement of the eye on the persistence of the after-image. In foveal vision, movement of the eye after exposure caused the after-image to disappear, while in extrafoveal vision movement had no effect. The author further believes that the cones are directly stimulated by light rather than by the decomposition products of visual purple. Morris Kaplan.

5

DIAGNOSIS AND THERAPY

Berke, R. N. **An operation for ptosis utilizing the superior rectus muscle.** Arch. Ophth. **42**:685-708, Dec., 1949.

This is a modification of the Motais technique combined with resection of the superior rectus muscle. First the superior rectus muscle is tenotomized and resecured to its stump so that 5 to 10 mm. of muscle project beyond the stump. This projecting portion of muscle is divided into three bundles and brought through an incision above the tarsus and sutured to the anterior tarsal surface. Postoperative hypotropia, a complication of the Motais procedure, is combatted by the resection of the superior rectus. Notching of the upper lid is prevented by dividing the superior rectus into three bundles and suturing them separately to the tarsus. Supplemental sutures prevent entropion and produce a normal-looking lid fold. This procedure is useful in ptosis where there is no levator action. It may be used even though the superior rectus is weak because the weakness is compensated for by the resection. Twenty illustrative cases are cited, including examples of paresis of the superior rectus, the Marcus Gunn phenomenon and ptosis associated with blepharophimosis. (16 figures.) John C. Long.

Bietti, G. B. **Use of paraaminosalicylic acid alone or in association with streptomycin in ocular tuberculosis: experimental and clinical investigations.** Arch. Ophth. **43**:431-445, March, 1950.

In the eye paraaminosalicylic acid exerts a tuberculostatic effect, which, unlike the sulfones it also does in nonimmune-allergic animals. Although the action of PAS seems inferior to streptomycin, the association of the two drugs gives a more intense effect than their use separately. After animal experimentation a clinical trial with 18 patients was performed. PAS was given in dosages of 10 to 12 grams daily, often in association with 0.5 to 1 grams of streptomycin in 20-day courses. The results were considered reasonably good and worthy of further trial. The author believes that oral PAS and intramuscular streptomycin, with the addition of PAS iontophoresis for lesions of the anterior segment, should be tried in every case of active ocular tuberculosis. In the doses now used the drugs are only bacteriostatic.

E. J. Swets.

Blatt, Nicolas. **Intraocular therapy with penicillin in syphilitic infections of the eye.** Arch. d'opht. **10**:62-64, 1950.

Blatt reports favorable results with penicillin in the treatment of 17 cases of syphilitic interstitial keratitis, 12 cases of fibrinous iridocyclitis, 6 cases of exudative choroiditis, and two syphilomas of the ciliary body. The penicillin was injected into the anterior chamber, or into the vitreous cavity, in infections of the choroid or ciliary body. The dosage varied from 500 to 1000 units and was adminis-

tered every 6 hours in the case of anterior chamber injection and every 10 to 12 hours in the case of intravitreous injection, over a period of several days. Retrobulbar injection of novocaine was used for anesthesia. No complications referable to the penicillin were noted. Similar cases failed to respond to penicillin administered by the conventional routes.

Phillips Thygeson.

Bonavolontá, Antonio, and de Berardinis, Elio. **Large doses of novocaine and penicillin by infiltration.** Rassegna ital. d'ottal. **19**:8-23, Jan.-Feb. 1950.

Clinical experience demonstrates that a single intra-muscular injection of 300,000 units of novocaine-penicillin in water maintains a satisfactory blood level for 24 hours. This is three times that obtained by penicillin in wax or oil. Toxic effects were not observed. The results of treatment of diseases of the eye not dependent on general causes were excellent. The antibiotic was injected into the region of the lacrymal sac, palpebral tissues and conjunctiva .There were no evidences of local intolerance or signs of general disturbance. The novocaine affords an immediate relief of pain which persists for several hours. The preparation was employed in diseases of the lacrymal passages, trachoma, pemphigus, corneal diseases and post-traumatic infections.

Eugene M. Blake.

Bucalossi, A. **Objective control of the dioptric function of the eye.** Atti d. 37 Congresso Soc. ital. oftal. **10**:66-71, 1948.

The author describes his new refractometer which combines the direct ophthalmoscope of Maggiore with the ophthalmometer of Badal.

Frederick C. Blodi.

Castroviejo, Ramon. **Suturing forceps for scleral, corneal and cataract work.** Tr. Am. Acad. Ophth. p. 372, March-April, 1950.

A modification of the St. Martin forcep, with the teeth set obliquely and with arms somewhat longer and stronger than the original model, is presented. Near the teeth are two flat surfaces which come into contact when the forcep is closed. Forceps with two sizes of teeth are available.

Gustav C. Bahn.

Chambers, B. M. **Treatment of giant follicular lymphoma with nitrogen mustard (methyl-bis-[2-chloroethyl] amine): report of a case.** Arch. Ophth. **43**:520-525, March, 1950.

An interesting case of giant follicular lymphoma of the right orbit with pathologic proof of a similar condition in the cervical lymph nodes is presented. A large mediastinal mass which did not regress with radiation therapy was also present. Complete regression of orbital and cervical tumors after the use of nitrogen mustard was noted objectively. Even if nitrogen mustard therapy is no more effective than radiation therapy, its use may be of value to the ophthalmologist who fears the hazards of irradiation of the eye.

E. J. Swets.

NEWS ITEMS

Edited by Donald J. Lyle, M.D.
601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received by the editor at least three months before the date of occurrence.

Deaths

Dr. Harvey Dansmore Lamb, St. Louis, Missouri, died April 6, 1950, aged 66 years.

Dr. Gideon McDonald Van Poole, Honolulu, Hawaii, died April 13, 1950, aged 73 years.

Miscellaneous

Ophthalmic equipment wanted

Dr. Victor Rambo, ophthalmic surgeon, Christian Medical College Hospital, Vellore, N.A., South India, is in dire need of ophthalmic instruments and drugs of all sorts to help take care of the enormous load of poor eye patients at this hospital. Anything of use will be gratefully received and appropriately used.

The supplies and instruments, which will then be forwarded to Dr. Rambo, can be sent to:

Mr. Harvey Tiedeck
Rambo Committee
1505 Fidelity Philadelphia Building
123 South Broad Street
Philadelphia 9, Pennsylvania

Gradle Memorial Services

On Saturday, June 10th, memorial services for the late Dr. Harry Searls Gradle were held at the American College of Surgeons Building, Chicago, Illinois. Mr. Chauncey McCormick of the Illinois Society for the Prevention of Blindness presided. The speakers were: Dr. Peter C. Kronfeld, University of Illinois; Dr. Thomas D. Allen, secretary of the Pan-American Association of Ophthalmology; Dr. William L. Benedict, executive secretary-treasurer of the American Academy of Ophthalmology and Otolaryngology; and Mr. Hugo Sonnenschein, Chicago, Illinois.

Launches research program

The National Council to Combat Blindness, Inc., launched its formal research program in the field of ophthalmology at a meeting of its medical board of consultants with the awarding of $15,366 in grants-in-aid to five universities and institutions. At this first meeting of the medical consultants, the program of the National Council to Combat Blindness, Inc., relating to the support and sponsorship of scientific study concerned with sight—both normal and pathologic—was unanimously endorsed.

The recipients of the awards for the year July 1, 1950, to June 30, 1951, are:

Boston City Hospital, granted $6,000, where Dr. Hermann M. Burian will conduct an investigation on the electrical responses of retina and brain in patients with amblyopia ex anopsia and supression.

New York Medical College, Flower and Fifth Avenue, granted $1,700, where Dr. Charles Haig will study the regional light sensitivity of the retina—technique and theory.

Northwestern University Medical College, granted $936, where Dr. Frank W. Newell will study quantitative measurements of ocular fluorescein fluorescence in normal and glaucomatous eyes.

Nuffield Laboratory of Ophthalmology, the Eye Hospital, Oxford University, England, granted $1,730, where Dr. Antoinette Pirie will investigate the normal and abnormal structures of the vitreous humor by microchemical and histochemical methods.

University of Pennsylvania, granted $5,000, where Dr. Harold G. Scheie will lead a study on virus infections of ocular tissues grafted onto the chorioallantoic membrane of the chick embryo.

A grants-in-aid committee was formed, consisting of: Dr. Phillips Thygeson, clinical professor of ophthalmology, University of California Medical College, chairman; Dr. Alson E. Braley, chief of department of ophthalmology, University Hospital, Iowa City; Dr. Dan M. Gordon, assistant professor, department of ophthalmology, Cornell University Medical College; Dr. Stuart Mudd, professor of bacteriology, School of Medicine, University of Pennsylvania; Dr. Charles A. Perera, assistant clinical professor of ophthalmology, College of Physicians and Surgeons, Columbia University; Dr. Samuel L. Saltzman, assistant clinical professor of ophthalmology, New York Medical College.

Announcements

College of Surgeons meeting

The International College of Surgeons, United States chapter, will hold its 15th annual assembly and convocation in Cleveland, Ohio, October 31, November 1, 2, 3, 1950, according to Dr. George M. Curtis, Columbus, Ohio, chairman of the assembly.

Dr. Arnold S. Jackson, secretary of the United States chapter, has reported from Madison, Wisconsin, that several hundred surgeons will be received as associates and fellows of the International College at the convocation to be held in the Cleveland Public Auditorium, November 3rd.

All doctors of medicine interested in surgery and its advancement are invited to attend, and can obtain a program upon request to Dr. Arnold S. Jackson, secretary, Jackson Clinic, Madison 4, Wis-

consin. For hotel reservations, contact Committee on Hotels, International College of Surgeons, U.S. Chapter, 511 Terminal Building, Cleveland 13, Ohio.

IV Pan-American Congress

The IV Pan-American Congress of Ophthalmology will be held in Mexico City from January 6 to 12, 1952.

Wills clinical conference

The third annual clinical conference of the Wills Eye Hospital, Philadelphia, Pennsylvania, will be held at the hospital, March 16 and 17, 1951.

As in other years, papers which reveal the latest developments in ophthalmic treatment and procedures will be presented by many of the nation's outstanding ophthalmologists.

Societies

AOS officers

Officers elected at the recent meeting of the American Ophthalmological Society are: President, Dr. John H. Dunnington, New York; vice-president, Dr. Lawrence T. Post, St. Louis; secretary-treasurer, Dr. Maynard C. Wheeler, New York; editor, Dr. Gordon M. Bruce, New York.

Pennsylvania Academy officers

Newly elected officers of the Pennsylvania Academy of Ophthalmology and Otolaryngology are: President, Dr. Jay G. Linn, Pittsburgh; president-elect, Dr. Matthew Ersner, Philadelphia; secretary, Dr. Daniel S. DeStio, Pittsburgh; treasurer, Dr. Bruce A. Grove, York.

Milwaukee society officers

The Milwaukee Oto-Ophthalmic Society held its annual meeting on May 22nd and elected the following officers for 1950-51: President, Dr. J. P. Wild; vice-president, Dr. B. P. Churchill; secretary-treasurer, Dr. Howard Hi[illegible]; directors: Dr. George Dunker, Dr. Samuel Bl[illegible]enstein, and Dr. F. Treskow.

The guest speaker, a British surgeon, Geoffrey A. Myers, F.R.C.S., chose as his subject "The future of private practice."

Resolutions passed by Florida society

At the recent meeting of the Florida Society of Ophthalmology and Otolaryngology, the following resolutions were passed by majority vote:

1. That the Florida Medical Association disapprove the advertising campaign carried on by the American Optical Company and that the American Optical Company desist from any further advertising of this character.

2. That the Florida Medical Association present bills before the Florida legislature: (a) That optometrists cannot examine eyes of individuals under 15 years of age; (b) if an optometrist's eye examination cannot bring vision up to 20/20 in both eyes, with binocular vision, that patient must be referred to an eye physician (ophthalmologist or oculist); (c) an optometrist is not permitted to treat any dysfunction of the eyes by prisms, exercises, contact lenses; (d) that the prices of eyeglasses can be advertised in newspapers, by radio, or by other modern means of advertising by registered opticians.

3. That the Florida Society of Ophthalmology and Otolaryngology send protests to the A.M.A., American Academy of Ophthalmology and Otolaryngology, and American Ophthalmological Society concerning unethical advertising of the American Optical Company.

Personals

Under the auspices of the Iran Foundation, Dr. R. Townley Paton, New York ophthalmologist and vice-president of The Eye-Bank for Sight Restoration, Inc., left for Iran on July 15th to study eye diseases and to make recommendations as to treatment. Particular emphasis of his survey will be placed on the prevention and treatment of trachoma and ophthalmia neonatorum. Dr. Paton is being sent as a member of the Medical Advisory Council, of which Dr. Allen Whipple is chairman.

Before going to Iran, Dr. Paton attended the XVI International Congress of Ophthalmology in London, England, where he presented the latest research developments at The Eye-Bank for Sight Restoration, Inc.

Upon his arrival in Iran, Dr. Paton will be met by His Excellency Sussien Ala, Minister of Foreign Affairs and president of the Iran Foundation.

Dr. Joseph I. Pascal presented a scientific exhibit on "A graphic study of the ocular muscles" at the XVI International Congress of Ophthalmology. Dr. Pascal is a delegate to the Congress from the New York Society for Clinical Ophthalmology.

After attending the XVI International Congress of Ophthalmology, Dr. Archie E. Cruthirds, Phoenix, Arizona, went to Edinburgh and Glasgow to attend sectional meetings of the Scottish Ophthalmological Society. From Scotland, Dr. Cruthirds flew to Buenos Aires where he presented a paper before the Argentine chapter of the International College of Surgeons.

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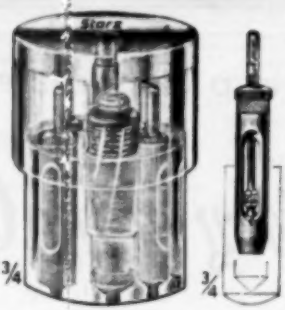

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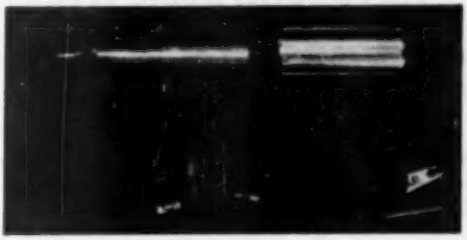

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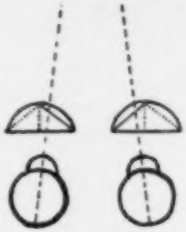

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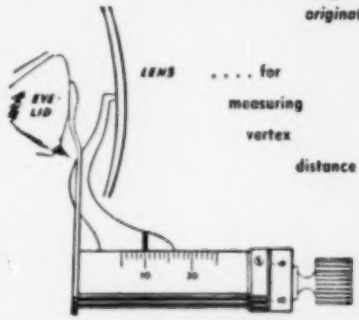

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1908 Ogden Avenue at Wolcott. (Formerly Belgard, Inc.)

109 N. Wabash, at Washington
9th Floor **STate 2-5362**

The NEW MONOPLEX *integrated* IMPLANT

The small, round cut-back neck permits purse-string suturing. Plastic lip protects area of conjunctiva where it is drawn around the neck. The placement of the tantalum mesh over a series of channeled grooves in the plastic simplifies suturing of the muscles and permits a firm attachment of tissue. The large area of smooth acrylic plastic on the posterior portion facilitates motility.

Simple symmetrical design

proven advantages

Write American Optical Company, Dept. CP-AM, Southbridge, Mass., for "Technique of Enucleation", Monoplex Implant, written by Dr. Jay G. Linn, Jr.

American Optical
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